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EXFOLIATIVE CYTOLOGY IN THE DIAGNOSIS OF CANCER

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The diagnosis of cancer by means of exfoliative cytology is based on the fact that malignant cells exfoliate more readily than their benign prototypes, and also on certain characteristics which these exfoliated malignant cells possess. In some cases these characteristics are so well marked that there is little doubt about the diagnosis; in many other cases however all that can be said of them is that their appearance is suggestive of malignancy. Even a doubtful report is useful because it indicates the need for further investigation by smears or biopsy. With increasing experience of the method comes an increasing number of definite reports both positive and negative, but even the most experienced cytologists are sometimes in doubt.

Cancer cells have been described by many writers (Papanicolaou, Graham, Farber, and others) but never more clearly than by Dudgeon, of St. Thomas's Hospital, London, who in 1934 wrote: 'Malignant cells stain more deeply than their benign prototypes. This is due to the fact that their nuclei have a greater affinity for haemalum. They vary in size and shape, they are larger than normal, and their position relative to the surrounding cytoplasm is in no way constant. The nuclear chromatin is arranged in thick irregular deeply-staining bundles and the fine reticular arrangement of normal cells is rarely seen. The nucleoli are larger than normal, they are sometimes multiple and stand out as prominent pink dots in the sphere of the nucleus'.[1] But no verbal description of malignant cells is adequate. Even good coloured photographs often leave much to be desired. They draw attention to certain features and in this way they are very helpful, but often it is necessary when examining malignant cells to focus up and down in order to get a proper appreciation of the cell. The information obtained in this way obviously cannot be portrayed by a microphotograph.

As a diagnostic method exfoliative cytology lends itself particularly to the diagnosis of cancer of the lung and cancer of the cervix. Its value in regard to other organs has yet to be critically assessed; Work on the subject is proceeding.

Cancer of the Lung

In cancer of the lung a proportion (20-25%) of the growths is beyond the view of the bronchoscopist and it is in these cases that the method finds its greatest use. It is little bother for even a very sick patient to provide the necessary sputum. Too often, however, saliva is submitted instead of sputum. It should be impressed upon the nurse, or whoever is collecting the specimen, that what is required is a deep cough sputum. It is wise to ask the patient first to swallow his saliva in order to avoid diluting the sputum. This also serves to remind both patient and attendant that it is the secretion from deep down in the lungs which is required. With patience a satisfactory specimen can be obtained in the vast majority of cases. Specimens showing the presence of blood are likely to be most helpful.

The sputum should be examined carefully, and as soon as possible, by the naked eye. This is best done by transferring it to a Petri dish. Then, with a loop, between 5 and 10 smears are made. In selecting portions for microscopical examination attention should be paid to blood-stained areas and also to any solid granules which may be seen in the specimen. Food particles which had been retained in the mouth may mislead, but in practice this does not happen often. The smears are fixed immediately while still wet. This may be done by placing the slides in a mixture of equal parts of 95% ethyl alcohol and ether, and then staining them by the Papanicolaou technique. The method preferred in this laboratory, however, is to place the smears in Schaudinn's solution and then stain them by the technique recommended by Dudgeon. In our experience Meyer's haemalum, which is employed in Dudgeon's method, gives the best nuclear definition; furthermore, it makes it possible to compare the cytological findings more easily with the subsequent histological examination. It must be stated, however, that the Papanicolaou method has decided advantages in the study of vaginal smears.

After staining, the preparations are mounted and examined from end to end in the manner of a histological section. Low power (2/3rds) is used, but all suspicious cells are scrutinised under high power (1/6th). A knowledge of the normal, or at least the benign, cells of the part is essential. While attention is mainly directed to the detection of malignant cells the presence of other cell elements is noted. A preponderance of simple squamous cells suggests dilution with saliva, the presence of lung histiocytes indicates that

the specimen did in fact come from 'deep down'. Considerable numbers of red cells may be present, even though blood was not visible grossly; this will provide indirect evidence of (*inter alia*) cancer. Other bodies may occasionally be seen; eg. cysts of *Entamoeba histolytica*, hooks of hydatid (C. W. Harington—personal communication) and fungal elements. In some cases the appearance of caseous material will indicate that smears should be stained by the method of Ziehl-Neelsen.

While sputum is the fluid most commonly examined in suspected cases of cancer of the lung, bronchial washings and pleural fluid, if available, sometimes give information of great value. These are centrifuged and smears prepared from the deposit. As with the sputum, the smears are fixed while wet and stained by a prescribed method.

It is not possible precisely to assess the value of this method in the diagnosis of lung cancer. There are two reasons for this. In the first place, it is not known if all cancers of the lung always exfoliate cells. There is evidence that some do not, and also evidence that some do so intermittently. In the second place, much depends upon the experience of the cytologist and the length of time he can allow himself to devote to the case. Nevertheless, while a precise assessment is impossible it can be confidently stated that in cytology we have an exceedingly valuable method for the diagnosis of lung cancer, which may well prove comparable to an examination of the sputum for acid-fast bacilli in the diagnosis of pulmonary tuberculosis. Furthermore, in exfoliative cytology we have a method which may disclose cancer of the lung even before radiological evidence of it is found—in fact, on occasions, even before clinical symptoms appear.

Cancer of the Cervix

The diagnosis of cancer of the cervix by means of exfoliative cytology was introduced by Papanicolaou in 1943 in the United States of America. The method is employed extensively in that country and to a lesser but increasing extent in Great Britain. As the cervix is so accessable to biopsy it had been suggested that a cytological examination of vaginal smears is redundant. There is weight in this argument. Nevertheless, as Bamforth has recently pointed out: 'The great advantage of the cytological method is that many early and unsuspected cases have been brought to light by it in the first place'.[2] Therein lies sufficient justification for the method. Furthermore, malignant cells originating in the cervix have been discovered in vaginal smears when initial biopsy of the cervix failed to reveal malignant growth. This procedure, therefore, is not a substitute for, but an adjunct to surgical biopsy.

Vaginal smears prepared from fluid in the posterior fornix, together with smears made from scrapings of the cervix, are fixed in the manner described for sputum. They are then stained and examined in the usual way. There is some doubt whether intra-epithelial carcinoma can be distinguished from invading carcinoma by this method. On this aspect of the subject Bamforth writes: 'I do not think that the cytological changes can indicate with certainty yet whether it is a case of invasive or non-invasive carcinoma; in order to decide this question one must have recourse to biopsy'.[3]

As in the diagnosis of cancer of the lung, it is not possible to state in precise terms the value of the method; there are many variable and unknowable factors concerned. However, the figures of Graham,[4] working in Boston, and Anderson *et al.*,[5] in Edinburgh, leave no doubt that the method is exceedingly valuable in capable hands. Nevertheless, a positive smear diagnosis should not be accepted as final until it has been confirmed by biopsy, which still remains the standard means for the diagnosis of cancer of the cervix.

Cancer of other Organs

While exfoliative cytology finds its greatest usefulness in the diagnosis of cancer of the lung and cancer of the cervix, its application is by no means limited to these organs. Table I shows the cancers in which this method of diagnosis is possible, together with the fluid used in each instance.

TABLE I. CANCERS WHICH LEND THEMSELVES TO DIAGNOSIS BY CYTOLOGY

Organ	*Fluid*
1. Breast	Discharge from nipple. Breast suckings.
2. Lung	Sputum. Pleural fluid. Bronchial suckings.
3. Cervix	Vaginal smear. Cervical scrapings.
4. Prostate	Prostatic secretion (during prostatic massage).
5. Bladder	Urine.
6. Kidney and Pelvis of Kidney	Urine (ureteric catheter).
7. Stomach	Fasting gastric juice. Gastric washings. Ascitic fluid.
8. Oesophagus	Fasting gastric juice. Oesophageal washings.
9. Colon	Ascitic fluid. Colonic washings.

At the present time, if cancer is to be cured at all, an early diagnosis is essential. In exfoliative cytology we have a technique which may, and often does, give the earliest indication of malignant growth.

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4. Graham, R. M. (1950): *Progress in Gynaecology*, 2nd ed., p. 133. London: Meigs and Sturgess.
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The San Michele Home for Mentally Defective Boys, Elandsfontein, District Boksburg, Transvaal, reported at its last annual meeting that, at a cost to date of £22,000, it had concluded a programme of new building making provision for a further 34 children, which would bring the total accommodation to 94. The Home caters for boys between the ages of 5 and 17 years who are physically and mentally retarded and cannot be accommodated in any other institution. Of the present inmates 20% are permanently bedridden and 16% semi-bedridden. Amongst the honorary medical staff are Dr. P. Kushlik, Dr. A. Segil, Dr. S. Friedman and Dr. C. B. Jeppe, with Dr. C. F. Geyer, dentist. The chairman is Mr. D. N. Murray.

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EDITORIAL

HASHIMOTO'S DISEASE, CLINICAL AND DIAGNOSTIC FEATURES

Several groups of workers in Britain have recently reported interesting findings in the previously obscure and neglected condition known as Hashimoto's goitre, or struma lymphomatosa, as the original author named it. It is likely that these findings will have interest and importance well outside the narrow thyroidal or even endocrinal sphere and may start new lines of investigation into the aetiology of other obscure disorders.* The recent work is well summarized in a series of communications made to the Royal Society of Medicine in 1957.

Hashimoto's disease is not at all uncommon, though usually mistaken for multinodular goitre or carcinoma on clinical examination. It is by far the most likely diagnosis in a patient of middle age who has hypothyroidism with a goitre, provided, as Luxton[1] points out, that goitrogenic substances can be excluded. This author stated that cases may occur from the 8th to 80th year, most patients being in their thirties, forties or fifties. In his series of 41 patients only 3 were male.

Describing the clinical picture further, Luxton[1] says that the goitre is usually, though not always, of recent origin—a matter of a year or so. It is not usually large, and may appear to be unilateral. It is usually firm, smooth and lobulated, and is not fixed. There may be mild pressure symptoms, hoarseness of the voice, and occasionally pain and tenderness. Sometimes the gland is relatively soft, or of variable texture. Lymph glands are not usually palpable. Luxton states that the goitre may be absent, but he does not elaborate further into how he would diagnose the condition under such circumstances.

The patient may be grossly myxoedematous when first seen, or may present the minor complaints of subthyroidism—feeling cold, 'rheumatic' aches and pains, and a general slowing down of mental and physical processes. Mental changes may be present, and Luxton states that the patients are very apprehensive and may at first refuse investigation or photography. Hypothyroidism is even more likely to develop after partial removal of the gland, as Hashimoto originally

* This subject will be further considered in an editorial in next week's issue of this *Journal*.

VAN DIE REDAKSIE

KLINIESE EN DIAGNOSTIESE ASPEKTE VAN HASHIMOTO SE SIEKTE

Verskeie groepe werkers in Brittanje het onlangs interessante bevindings gerapporteer oor die voorheen onbekende en verwaarloosde kondisie bekend as die Hashimoto-krop, of struma lymphomatosa, soos die oorspronklike beskrywer dit genoem het. Dit is moontlik dat hierdie bevindings van belang en betekenis sal wees ver buite die beperkte sfeer van die skildklier of selfs die endokrienstelsel, en kan beteken dat nuwe rigtings ingeslaan sal word in die navorsing op die etiologie van ander obskure siektes.* Die onlangse werk is raak opgesom in 'n reeks verslae gerig aan die *Royal Society of Medicine* in 1957.

Hashimoto se siekte is glad nie seldsaam nie, hoewel dit gewoonlik by kliniese ondersoek verkeerd aangesien word vir veelknobbelige kropgeswel of karsinoom. Dit is verreweg die waarskynlikste diagnose in die geval van 'n middeljarige pasiënt met gebrekkige skildklierwerking en 'n kropgeswel mits, soos Luxton[1] aantoon, stowwe wat aanleiding gee tot kropgeswel uitgesluit kan word. Hierdie skrywer het beweer dat die siekte tussen die 8ste en 80ste jaar kan voorkom; die meeste pasiënte is tussen 30 en 50 jaar oud. Slegs 3 van sy reeks van 41 pasiënte was mans.

In sy verdere beskrywing van die kliniese beeld, meld Luxton[1] dat die kropgeswel gewoonlik, dog nie altyd nie, van onlangse oorsprong is; dit het gewoonlik 'n jaar of wat tevore ontstaan. Gewoonlik is dit klein, en dit kan eensydig voorkom. Dit is gewoonlik ferm, glad en gelob, en sit nie vas nie. Daar kan ligte druksimptome, heesheid van stem, en soms pyn en teerheid wees. Soms is die klier betreklik sag, of van wisselende tekstuur. Gewoonlik is limfkliere nie betasbaar nie. Luxton sê dat die kropgeswel ook afwesig kan wees, maar hy verstrek geen verdere besonderhede oor hoe hy die kondisie onder sulke omstandighede sou uitken nie.

Die pasiënt kan by die eerste ondersoek ernstige miksedeem toon of hy kan presenteer met die minder ernstige klagtes van subtiroïedisme—'n gevoel van koue, ‚rumatiekpyne', en 'n algemene vertraging van geestelike en liggaamlike aktiwiteite. Geestesveranderings kan voorkom, en Luxton meld dat die pasiënte baie skrikkerig en angstig is en in die begin weier om ondersoek of afgeneem te word. Hipotiroïedisme kan selfs nog makliker ontwikkel ná gedeeltelike verwydering van die klier, soos Hashimoto oorspronklik uitgevind het. Soms toon die pasiënt kenmerkende skildkliervergiftiging, met die oogverskynsels; basale metabolisme-spoede van +69% is reeds gerapporteer.

* Hierdie onderwerp word verder bespreek in 'n hoofartikel in die volgende uitgawe van hierdie *Tydskrif*.

found out. Sometimes the patient has characteristic thyrotoxicosis, with eye signs; BMR up to +69% have been recorded.

Luxton believes that the abdominal viscera may be involved in Hashimoto's disease, and he describes one case which he would like to call 'Hashimotosis of the liver'. He found palpable spleens in several other cases, and occasionally some evidence of nephropathy. In 2 cases an actual nephrotic syndrome occurred. Another unexpected association was with Paget's disease; 7 of 35 patients had this bone disease in addition. Following on the interest in visceral involvement Luxton and Cooke[2] studied the liver function tests in Hashimoto's disease and found abnormal flocculation tests in 14 out of 16 untreated cases. After treatment with thyroid extract, only 1 patient out of 18 had abnormal flocculation tests. This interesting reversal of flocculation tests underlines the fact that thyroid administration seems the best treatment in Hashimoto's disease, not only for the hypothyroidism, but also to produce a reduction in the size of the goitre, and to alleviate any pressure symptoms. The thyroid should not be removed, provided the diagnosis is correctly made.

Doniach and his colleagues further discuss the diagnosis of Hashimoto's disease. In the early stages the BMR and 24-hour uptake of ^{131}I may be normal, unless thyrotoxicosis is present. As the degree of thyroid destruction increases, the output of thyroid hormone diminishes and the production of thyrotropic hormone (TSH) by the pituitary is increased. The ^{131}I uptake is now well above normal, while the BMR is maintained. Later the gland is unable to make enough thyroid hormone despite being stimulated by excessive amounts of TSH, and the BMR becomes subnormal though the ^{131}I uptake remains high. Finally even the iodine uptake gradually falls below normal. It is plain, therefore, that an apparent discrepancy between BMR (or the hypothyroid features) and ^{131}I uptake may exist, and this may be very useful in diagnosis. The only other untreated thyroid condition in which low BMR is combined with high ^{131}I uptake is familial non-endemic goitrous cretinism, in which a congenital absence of certain enzymes leads to an insufficiency of thyroid hormone. Other tests involving radio-active iodine in Hashimoto's disease indicate that the 48-hour plasma radio-activity is high even in association with myxoedema, and the iodine uptake cannot be increased by injections of TSH.

In distinction from carcinoma of the thyroid, the gammaglobulin and flocculation tests are normal in the latter (as they are also in multinodular colloid goitre). Doniach considers the most useful differentiating test is the topographical survey of iodine distribution over the goitre area. Hashimoto's disease, being a diffuse process, gives an isocount picture which usually follows the outline of the palpable swelling, whereas in carcinoma of the thyroid the uptake is usually asymmetrical and is absent over the tumour itself.

1. Luxton, R. W. (1957): Proc. Roy. Soc. Med., **50**, 943.
2. Luxton, R. W. and Cooke, R. T. (1956): Lancet, **2**, 105.
3. Doniach, D., Hudson, R. V. and Roitt, I. M. (1957): Proc. Roy. Soc. Med., **50**, 946.

Luxton meen dat die buikingewande ook aangetas kan word by die Hashimoto-siekte, en hy beskryf 'n geval wat hy graag ‚Hashimotose van die lewer' sou noem. Hy het by verskeie ander gevalle 'n tasbare milt teëgekom, en soms ook tekens van nieraantasting. By 2 pasiënte was daar 'n werklike nefrotiese sindroom. Dit is verder ook bevind dat daar 'n onverwagte verband bestaan tussen hierdie siekte en Paget se siekte; 7 uit 35 pasiënte het buiten die Hashimoto-siekte ook aan hierdie beenkwaal gely. Aangespoor deur hul belangstelling in ingewand-aantasting, het Luxton en Cooke[2] die lewerfunksie-toetse by Hashimoto se siekte bestudeer en bevind dat die uitvlokkingtoetse by 14 uit 16 onbehandelde gevalle abnormaal was. Maar na behandeling met tiroïed-ekstrak het slegs 1 uit 18 pasiënte abnormale uitvlokkingtoetse gelewer. Hierdie interessante omkering van die uitvlokkingtoetse beklemtoon die feit dat die beste behandeling vir Hashimoto se siekte blykbaar toediening van skildklier-ekstrak is, nie alleen vir die hipotiroïedisme nie, maar ook om die kropgeswel te krimp en die druksimptome wat mag voorkom te verlig. Die skildklier moet nie verwyder word nie—mits die diagnose korrek is.

Doniach[3] en sy medewerkers bespreek die diagnose van Hashimoto se siekte verder. In die vroeë stadiums kan die basale metabolisme-spoed en die ^{131}I-opname oor 24 uur normaal wees, tensy daar skildkliervergiftiging is. Namate die graad van skildkliervernietiging toeneem, verminder die uitstorting van die tiroïedhormoon, en vermeerder die vervaardiging van die tirotropiese hormoon (TSH) deur die harsingslymklier. Die ^{131}I-opname is dan heelwat bo die normale terwyl die basale metabolisme-spoed onveranderd bly. Later is die klier nie meer in staat om genoeg skildklierhormoon te vervaardig nie, nieteenstaande die feit dat dit geprikkel word deur oormatige hoeveelhede TSH; die basale metabolisme-spoed daal benede die normale, hoewel die ^{131}I-opname hoog bly. Uiteindelik daal selfs die jodium-opname geleidelik benede normaal. Dit is dus duidelik dat daar 'n oënskynlike teenstrydigheid kan bestaan tussen die basale metabolisme-spoed (of tekens van skildkliergebrek) en die ^{131}I-opname, en hierdie feit kan van veel betekenis wees by die diagnose. Die enigste ander onbehandelde skildkliersiekte waar 'n lae grondstofwisselingspoed gepaard gaan met 'n hoë opname van ^{131}I is familiale nie-endemiese krop-kretinisme, waarby 'n aangebore totale afwesigheid van sekere ensieme veroorsaak dat te min tiroïedhormoon afgeskei word. Ander toetse by die Hashimoto-siekte waarby radioaktiewe jodium gebruik word, toon aan dat die 48-uurlikse plasma-radioaktiwiteit hoog is, selfs al kom miksedeem voor, en die jodium-opname kan nie vermeerder word deur TSH in te spuit nie.

Anders as by skildklierkarsinoom is die gammaglobulien- en uitvlokkingtoetse normaal (hulle is ook normaal by veelknobbelige kolloidale krop). Doniach meen dat die topografiese berekening van jodiumdistribusie oor die krop-area die nuttigste onderskeidingstoets is. Omdat Hashimoto se siekte 'n toestand is wat versprei is, lewer dit 'n iso-telling-beeld wat gewoonlik die lyn van die tasbare geswel volg, terwyl die opname by karsinoom van die skildklier gewoonlik oneweredig is en oor die gewas self afwesig is.

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STUDIES ON THE REGULATION OF THE SERUM-CHOLESTEROL LEVEL IN MAN

SERIAL SERUM-CHOLESTEROL DETERMINATIONS IN ACTIVE MEN ON THEIR ORDINARY DIETS AND THE LONG-TERM EFFECT OF CERTAIN SATURATED- AND UNSATURATED-FAT SUPPLEMENTS*

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The influence of dietary fats on the serum cholesterol is being studied intensively and it is now well established that the quality of a fat determines its effect on the human serum-cholesterol level. It has been repeatedly confirmed that while certain saturated fats increase the serum-cholesterol level, some highly unsaturated fats decrease it. The effects of these fats, however, have only been demonstrated in artificial circumstances, viz. in acute dietary experiments,[1, 2] or with the use of drastically modified or unnatural 'formula' diets,[3-5] or in patients confined to hospital on standardized diets.[6, 7]

Hence we have set out to investigate the effects of dietary fats for extended periods in men consuming their accustomed diets and continuing with their usual business and recreational pursuits. Before such a study could be undertaken it was necessary to assess the 'spontaneous' fluctuations in the serum-cholesterol level of our subjects under ordinary living conditions. This communication deals with a group of 30 men in whom week-to-week fluctuations in the serum-cholesterol level have been studied and it presents a preliminary account of the influence of dietary fat supplements and other factors on the serum-cholesterol level of some of these men.

PLAN OF INVESTIGATION

The 30 subjects (Table II) were all European men and included clerical workers, professional men and business executives. Their ages ranged from 25 to 59 years with a mean of 43·1 years. Six of the men had previously sustained a cardiac infarction and, of these, 4 remained with mild angina pectoris but were free from cardiac failure. One man had peripheral arterial disease with slight intermittent claudication and another had xanthelasma palpebrarum with hypercholesterolaemia. The remaining 22 men were healthy as judged by clinical examination, urine analysis, blood count, blood-urea level and electrocardiograph.

The men were asked not to modify their diets or their activity throughout the trial. They attended a special clinic held in the early morning once a week at the Groote Schuur Hospital. Their regular attendance was only occasionally broken by illness or by business or holiday trips away from the Cape. During the early stages of the investigation, the subjects took no breakfast before attending the clinic; later, a light breakfast was permitted, as single meals are known not to influence the serum-cholesterol level.[8, 9]

At each attendance the subject's weight and blood pressure were recorded and a sample of blood was taken for serum-cholesterol determination. Variations in the diet, physical activity, bowel habits and general health were noted. The initial control period lasted, on the average, 13 weeks, during which an average of 10 serum-cholesterol determinations were made. At the end of this period, various fats were given to the subjects to take as supplements to their regular diet.

The fats used, their dosage and the length of time they were consumed are indicated in Tables IV, V and VI. The fats were usually taken in 2 doses daily, at the subject's convenience in relation to meals. The oils were drunk raw; the solid fats were melted and drunk or combined with the food. The oils were generally taken for long periods, averaging 6 months; in a few cases, when the subject had to leave home for long business or holiday trips, the oils were given for shorter periods. The subjects who consumed the saturated fats were generally younger men and the period of administration was much shorter.

Subject 15 consumed 240 g. of dehulled sunflower seeds daily in addition to his regular diet. These contain about 45% of sunflower-seed oil. Subject 21 was not given any dietary supplement; instead he went onto a strict low-calorie diet. This diet was not rigorously controlled; it provided about 1,200 calories daily and was low in both fat and carbohydrate.

At the end of the fat-supplement period, the weekly observations continued during a second control period until the serum cholesterol level reached a steady state.

The iodine values of the fats and their sources are shown in Table I.

The analytical methods used were the following:

1. *Serum cholesterol:* Method of Abell *et al.*,[10] as modified by Anderson and Keys.[11] The reproducibility of the method was checked in our laboratory 3 times during the last year, on batches of 75-100 duplicate samples. The standard error of the method on each of these occasions was 3·9 mg.%, 4·2 mg.% and 3·8 mg.% respectively.

2. *Iodine value:* Macro-Wijs technique (A.O.C.S. official method Cd. 1-2).

Statistical Methods. To assess the spontaneous fluctuations of the serum cholesterol for each subject under the conditions of this study all the readings during the first control period were utilized. In subject 2, whose first control period was inadequate,

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TABLE I. THE FATS USED IN THIS INVESTIGATION

Fat	Iodine Value	Remarks
Pilchard oil	180	Derived from the South African pilchard (*Sardina ocellata* Jenyns) and supplied by Marine Oil Refiners, Simonstown, Cape.
'Lipidex'	135-140	A blend of vegetable oil extracts, emulsified and flavoured, supplied by Grey Pharmaceutical Co. Inc., Mass., U.S.A.
Sunflower-seed oil ..	132-136	This oil has been refined, winterized and deodorized. A number of batches of fairly constant iodine values have been used; these were supplied by Cape Oil Products, Maitland, Cape.
Maize oil	120	This refined oil was supplied by Lever Bros., Durban.
Hydrogenated sunflower-seed oil.	74	Supplied by Lever Bros., Durban.
Butter	42-46	Several batches of commercial butter were used.
Hydrogenated coconut fat	6	Supplied by Marine Oil Refiners, Simonstown, Cape.

the readings of a later control period were utilized. For assessing the effects of the fat supplements, in subjects 1-10 and 16-19, the mean serum-cholesterol level of the first control period was compared with the mean of the last 4 readings of the fat-supplement period, i.e. when the serum-cholesterol level has become more or less stabilized on the new regime. These data for the fat-supplement period were again compared with similar data derived from the last 4 readings of the second control period.

The following formulae were used:

1. S^2=variance of a subject's serum-cholesterol level

$$= \frac{\Sigma x^2 - \frac{(\Sigma x)^2}{n}}{n-1}$$

where n = number of readings of the serum cholesterol
x = individual values for serum cholesterol.

2. S=standard deviation of a subject's serum-cholestreol level.

3. Pooled standard deviation of the serum cholesterol for all the subjects studied

$$= \sqrt{\frac{\Sigma(n-1)S^2}{\Sigma(n-1)}}$$

4. Coefficient of variation for each subject $= \frac{S}{\bar{x}} \times 100$ where $\bar{x}$=mean serum-cholesterol level.

5. For each group of individuals, the significance of the difference between the means of the serum-cholesterol level for each of the two control periods and the fat-supplement period was calculated according to this formula

$$t_{(n-1)} = \frac{\Sigma \triangle}{\sqrt{nS_{\triangle}^2}}$$

where $\triangle$=difference between the means for each subject
$S_{\triangle}$=variance of the difference
n=number of subjects.

6. For each individual, the significance of the difference between the means of the serum-cholesterol level for each of the two control periods and the fat-supplement period was calculated as follows:

$$t_{(n+n'-2)} = \frac{\bar{x} - \bar{x}'}{\sqrt{\left(\frac{n+n'}{nn'}\right)\frac{(n-1)S^2+(n'-1)S'^2}{n+n'-2}}}$$

where $\bar{x}$ and $\bar{x}'$ are the mean serum-cholesterol levels for each period
n and n' are the numbers of readings of the serum-cholesterol in each period
S and S' are variances of the serum-cholesterol level in each period.

RESULTS

Fluctuations in the Serum Cholesterol during the Control Period

In the 30 subjects studied, from 6 to 18 determinations of the serum-cholesterol level have been made in each, with an average of 10·5 determinations per subject. These estimations were made during periods of 6 to 34 weeks (average 13 weeks per subject). The data are summarized in Tables II and III. The intra-individual fluctuations have been analysed in a number of ways, as follows:

1. *The intra-individual range of the serum-cholesterol level,* i.e. the difference between each subject's highest and lowest values, varied from 26 to 96 mg.%, with an average for the group of 45 mg.%.

TABLE II. THE MATERIAL OF THIS INVESTIGATION AND THE INTRA-INDIVIDUAL FLUCTUATIONS IN THE SERUM-CHOLESTEROL LEVELS OF THE 30 SUBJECTS WHILE ON ORDINARY DIETS AND NORMAL ACTIVITY

Subject	Age (years)	Clinical Status	Duration of Observation (weeks)	No. of Readings	Lowest and Highest Values (mg.%)	Range (mg.%)	Mean Level (mg.%)	Standard Deviation of Mean (mg.%)	Maximum Deviation from Mean (%)	Coefficient of Variation (%)
1	56	C	16	11	225 258	33	244	9·8	7·8	4·1
2	41	C	13	11	306 347	41	321	13·0	7·9	4·0
3	49	N	34	10	187 230	43	215	14·2	13·0	6·6
4	55	N	9	7	213 274	61	244	20·4	12·3	8·4
5	53	N	18	14	220 262	42	239	12·8	9·6	5·3
6	33	N	9	8	185 238	53	220	16·0	15·9	7·3
7	47	C	15	13	207 257	50	239	14·7	14·4	6·1
8	46	N	23	18	230 301	71	260	17·9	15·8	6·9
9	43	N	15	13	224 262	38	246	12·0	9·0	4·9
10	59	C	13	9	211 240	29	220	8·2	9·1	3·7
11	35	N	13	10	139 173	34	157	10·2	11·5	6·5
12	51	N	19	14	193 264	71	216	19·0	22·2	8·8
13	45	N	14	12	193 233	40	213	13·9	9·4	6·5
14	57	C	10	10	244 340	96	299	29·6	18·4	9·9
15	25	N	12	10	259 298	39	283	13·1	8·5	4·6
16	27	N	10	10	150 185	35	169	11·4	11·3	6·7
17	27	N	10	10	130 194	64	175	19·4	25·7	11·1
18	35	N	10	10	166 209	43	187	13·7	11·7	7·3
19	30	N	10	10	182 208	26	196	9·4	7·1	4·8
20	44	N	24	21	179 229	50	210	12·4	14·8	5·9
21	46	N	10	11	202 259	57	228	16·5	13·6	7·2
22	45	X	6	6	360 398	38	373	13·7	6·7	3·7
23	46	C	6	7	356 395	39	371	14·5	6·5	3·9
24	55	N	15	11	243 286	43	267	13·9	9·0	5·2
25	42	N	6	6	194 229	35	216	12·0	10·2	5·5
26	48	N	12	9	197 231	34	215	9·4	8·4	4·4
27	48	P	8	8	225 274	49	256	18·2	12·1	7·1
28	41	N	7	7	239 272	33	255	10·4	6·7	4·1
29	38	N	8	8	182 204	22	193	7·7	5·7	3·9
30	26	N	14	12	181 215	34	197	11·0	9·1	5·6

N=normal. C=coronary heart disease. X=xanthelasma. P=peripheral arterial disease.

TABLE III. SUMMARY OF INTRA-INDIVIDUAL FLUCTUATIONS RECORDED IN TABLE II

	Minimum	Maximum	Mean
Age (years)	25	59	43·1
Duration of Observation (weeks)	6	34	13·0
Number of Readings	6	21	10·5
Mean Serum-cholesterol Level (mg.%) ..	157	321	237·4
Standard Deviation (mg.%)	7·7	29·6	14·7
Intra-individual Range (mg.%)	22	96	44·8
Maximum Deviation from Mean (per cent) ..	5·7	25·7	11·4
Coefficient of Variation	3·6	10·9	6·0

2. *The maximum deviation of the serum-cholesterol from the mean value* varied among the subjects from 6% to 22%, with a mean for the group of 11·9%.

3. *The standard deviation of the serum-cholesterol level* of each subject varied from 7·7 mg.% to 29·6 mg.%. Pooling of the standard deviations for all 30 subjects gave a value of 14·7 mg.%.

4. *The coefficients of variation* have been calculated to compare the fluctuations among the 30 subjects. These vary from 3·6% to 10·9% with an average for the group of 6·1%.

The Effect of Unsaturated-fat Supplements

These supplements have been studied in 18 men. In 4 of these (subjects 22-25) the trial is not yet complete and 4 others have withdrawn from the trial, 2 (subjects 11 and 12) because they gained too much weight and 2 (subjects 13 and 14) because they were unable to tolerate the oil. The results in the remaining 10 men are shown in Table IV. Figs. 1-5 are representative illustrations.

It will be seen that the mean serum cholesterol of this group fell from the first control level of 247 mg.% to 213 mg.% by the end of the fat-supplement period. The difference, 34 mg.%, is highly significant. Individual decreases in the serum-cholesterol level ranged from 2 to 87 mg.%. In 8 cases, the decrease was statistically significant, in subject 3 the change of 17 mg.% had no statistical significance, and in subject 10 the daily consumption of 50 g. of sunflower-seed oil for 29 weeks had no appreciable effect on the serum-cholesterol level.

The pattern of response varied in these subjects. In 6 of them there was a slowly progressive decrease in the serum-cholesterol level, which became stabilized after 2-3 months (Figs. 2 and 3). In the other two who responded there was an initial sharp fall, which was maintained throughout the fat-supplement period (Fig. 1). In none of these subjects was the fall in serum cholesterol followed by a secondary rise while the subject was still consuming the oil supplement.

Since the end of the second control period, subjects 1, 3, 4, 7 and 10 have completed a further period on an unsaturated-fat supplement, lasting about 6 months. The nature of the supplement and the changes in the serum-cholesterol level are indicated in Table V. Significant decreases in the serum-cholesterol level were again recorded by subjects 1, 3, 4 and 7 but in subject 10, once more, 50 g. of maize oil daily for 25 weeks failed to influence the serum-cholesterol level (Figs. 2 and 4).

Side-effects of the Unsaturated-fat Supplements. Subjects 13 and 14 developed nausea, distension and anorexia when they took 50 g. of sunflower-seed oil daily. Emulsifying the oil in water (with powdered tragacanth) and embellishing it with synthetic ginger, strawberry or orange flavours did not improve its acceptability to these two men and they withdrew from the trial. None of the other subjects found the oils pleasant to take but they soon became accustomed to drinking them. The only symptom which could be attributed to the

TABLE IV. THE EFFECT OF A DAILY SUPPLEMENT OF UNSATURATED FAT ON THE SERUM-CHOLESTEROL LEVELS OF 10 MEN

First Control Period						*Fat-supplement Period*						*Second Control Period*			
Subject	*Age*	*Duration (weeks)*	*No. of Readings*	*Mean Serum Cholest. (A) mg.%*	*Standard Deviation of A*	*Fat*	*Dose (g.)*	*Duration (weeks)*	*Mean Serum Cholest. (B) mg.%*	*Difference (A-B) mg.%*	*Significance of Difference (p)*	*Duration (weeks)*	*Mean Serum Cholest. (C) mg.%*	*Difference (C-B) mg.%*	*Significance of Difference (p)*
1	56	16	11	244	9·8	SSO	50	33	217	−27	<0·001	13	232	+15	<0·01
2	41	3	3	340	11·5	PO or SSO	75	32	253	−87	<0·001	24	322	+69	<0·001
3	49	34	10	215	14·2	SSO	50	33	198	−17	<0·1	12	229	+31	<0·02
4	55	10	8	244	20·4	SSO	50	22	213	−31	<0·02	16	249	+36	<0·001
5	53	18	14	239	12·8	SSO	50	22	214	−25	<0·01	7	252	+38	<0·001
6	33	10	8	220	16·0	SSO	50	14	192	−28	<0·01	13	224	+32	<0·001
7	47	14	13	239	14·7	SSO	50	27	186	−53	<0·001	9	237	+51	<0·001
8	46	23	18	260	17·9	Lx	37	19	212	−48	<0·001	6	260	+48	<0·01
9	43	15	12	246	12·0	SSO	50	10	232	−14	<0·05	21	242	+10	<0·3
10	59	12	9	220	8·2	SSO	50	23	218	− 2	—	17	224	+ 6	<0·4
Mean		15·5	10·5	247				23·5	213	−34	<0·01	13·8	246	+33	<0·001

SSO = Sunflower-seed oil. PO = Pilchard oil. Lx = 'Lipidex'.

TABLE V. THE EFFECT OF A SECOND SUPPLEMENT OF UNSATURATED FAT ON THE SERUM-CHOLESTEROL LEVELS AND BODY WEIGHT OF 5 MEN. (The effects of the first supplement are recorded in Tables IV and VI)

Subject	*Second Control Period*		*Second Fat-supplement Period*						
	Mean Serum Cholest. (C) mg.%	*Body Weight (lb.)*	*Fat*	*Dose (g.)*	*Duration (weeks)*	*Mean Serum Cholest. (D) mg.%*	*Difference (C-D) mg.%*	*Body Weight (lb.)*	*Change in Weight (lb.)*
1	232	188	Lx	37	30	215	−17	193	+5
3	229	166	MO	50	21	206	−23	170	+6
4	249	156	MO or Lx	50 37	21	195	−54	160	+4
7	237	158	MO	50	22	204	−33	168	+10
10	224	163	MO	50	25	230	+ 6	172	+9
Mean	234	166·2			24	210	−24	180·6	+6·4

Lx = Lipidex. MO = Maize oil.

TABLE VI. THE EFFECT OF A DAILY SUPPLEMENT OF SATURATED FAT ON THE SERUM-CHOLESTEROL LEVELS OF 4 MEN

		First Control Period				Fat-supplement Period						Second Control Period			
Subject	Age	Duration (weeks)	No. of Readings	Mean Serum Cholest. (A) mg.%	Standard Deviation of A	Fat	Dose (g.)	Duration (weeks)	Mean Serum Cholest. (B) mg.%	Difference (B-A) mg.%	Significance of Difference (p)	Duration (weeks)	Mean Serum Cholest. (C) mg.%	Difference (B-C) mg.%	Significance of Difference (p)
16	27	10	10	169	11·4	HCF	50	5	195	+26	<0·001	5	166	−29	<0·01
17	27	10	10	175	19·4	HCF	50	5	225	+50	<0·001	5	194	−31	<0·01
18	35	10	10	187	13·7	HCF	50	5	227	+40	<0·001	5	182	−45	<0·01
19	30	10	10	196	9·4	HCF	50	5	213	+17	<0·02	5	197	−16	<0·1
Mean		10	10	182				5	215	+33	<0·02	5	185	−30	<0·02

HCF = Hydrogenated coconut fat.

oil was variable mild constipation. The transient episodes of diarrhoea which we have previously reported in the metabolism ward[12] have not been encountered in the present series. Subject 15 was unable to tolerate sunflower-seed oil because of nausea and distension. Nevertheless he consumed with relish 240 g. of dehulled sunflower seeds daily and his serum-cholesterol level fell from 265 to 220 mg.% (Fig. 5).

Effect on Body Weight. Throughout the trial period the subjects claimed to be following the instruction to take the fats as supplements and not to be modifying their regular

TABLE VII. THE SAME SUBJECTS AS IN TABLE IV, SHOWING THE EFFECT OF THE UNSATURATED-FAT SUPPLEMENT ON THE BODY WEIGHT

Subject	First Control Period	Fat Supplement Period		Second Control Period	
	Final Weight	Final Weight	Change	Final Weight	Change
1	195	192	−3	188	−4
2	202	217	+15	213	−4
3	160	163	+3	166	+3
4	158	160	+2	156	−4
5	165	164	−1	162	−2
6	212	216	+4	214	−2
7	163	157	−6	158	+1
8	181	187	+6	184	−3
9	206	210	+4	208	−2
10	152	164	+12	163	−1
Mean ..	179·4	183·0	+3·6	181·2	−1·8

diet. A study of their weight changes (Table VII), however, shows that they were in fact not gaining weight as would have been expected. Thus, only subjects 2 and 10 gained much weight, while subject 7 actually lost 6 lb. Similarly, during the second control period, the fall in weight was slight. It will be recalled that subjects 11 and 12 gained weight so rapidly on starting the oil supplement that they withdrew from the trial.

The Effect of the Saturated Fats

The results in subjects 16-19, who consumed 50 g. of hydrogenated coconut fat daily for 5 weeks, are shown in Table VI and Fig. 6. It will be noted that this group of men were younger than the previous group (mean age: 30 years) and that their initial serum-cholesterol level was relatively low (mean 182 mg.%). During the fat-supplement period, all the subjects showed significant increases in the serum-cholesterol level and the mean increase for the group (33 mg.%) was highly significant. On stopping the fat, the serum-cholesterol level fell from a mean of 215 mg.% to 185 mg.%; this change of 30 mg.% is also statistically significant.

Subject 20 (Fig. 7) showed clear increases in his serum-cholesterol levels during two fat-supplement periods, in which he consumed 75 g. of hydrogenated sunflower-seed oil and 50 g. of butter, respectively. At the end of each fat-supplement period, the serum-cholesterol level returned towards the control level.

None of these subjects experienced any untoward effect from the fat supplements. As with subjects consuming

TABLE VIII. THE SAME SUBJECTS AS IN TABLE VII, SHOWING THE EFFECT OF THE SATURATED-FAT SUPPLEMENT ON BODY WEIGHT

Subject	First Control Period	Fat Supplement Period		Second Control Period	
	Final Weight	Final Weight	Change	Final Weight	Change
16	139	141	+2	137	−4
17	130	134	+4	134	0
18	157	162	+5	159	−3
19	173	173	0	173	0
Mean ..	149·7	152·5	+2·8	150·7	−1·8

unsaturated fats, the gains in weight during the supplement periods were less than had been anticipated, again suggesting an unconscious restriction of intake at this stage (Table VIII).

The Relation of Changes in Body Weight to Changes in the Serum-cholesterol Level

The effect of weight reduction in subject 21, who was obese, is recorded in Fig. 8. It will be noted that on two occasions drastic caloric restriction produced marked and sustained falls in weight. With each episode of rapid weight loss, there was only a transient fall in the serum-cholesterol level. In fact, despite a loss of 30 lb. of body weight, at the

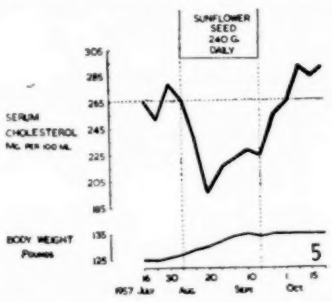

Fig. 5. Subject 15. A sharp fall in the serum-cholesterol level and a substantial gain in weight occurred when sunflower seeds were consumed.

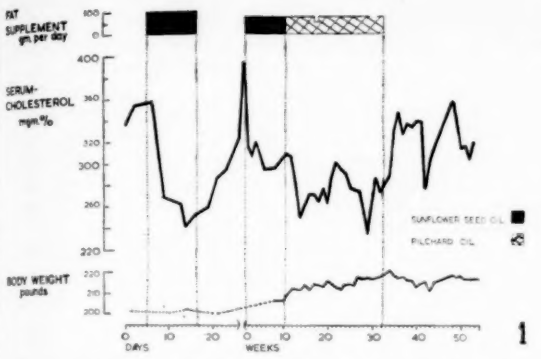

Fig. 1. Subject 2. During the first part of the investigation, the subject was in hospital; 100 g. of sunflower-seed oil daily for 12 days produced a prompt fall in his serum-cholesterol level. On discharge from hospital, his serum-cholesterol level was recorded weekly and its reduction was maintained for 32 weeks by the use of 75 g. supplements of sunflower-seed oil or pilchard oil. The reduction in serum-cholesterol level was accompanied by a marked increase in weight.

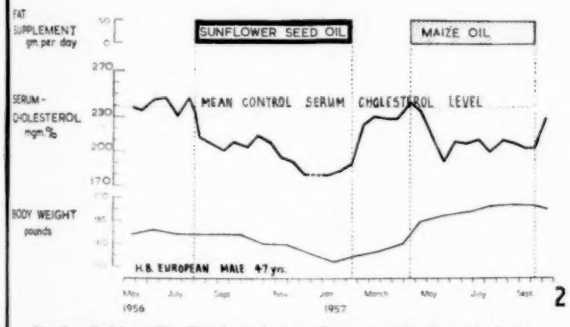

Fig. 2. Subject 7. During the sunflower-seed-oil period the fall in serum-cholesterol level was accompanied by a loss of weight; during the maize-oil period, it was accompanied by an increase in weight. (Each point on the serum-cholesterol graph represents the mean of 2 consecutive readings of the serum-cholesterol level.)

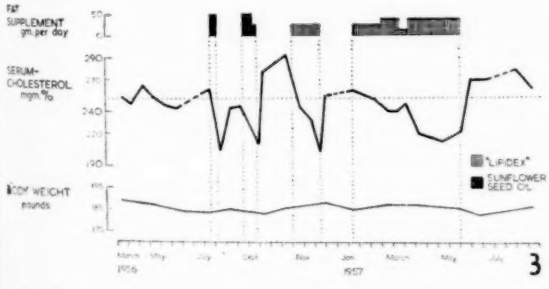

Fig. 3. Subject 8. Short courses of sunflower-seed oil and 'lipidex' produced prompt decreases in the serum-cholesterol level. The decrease was sustained when a 'lipidex' supplement was taken for 19 weeks. Serum cholesterol recorded as in Fig. 2.

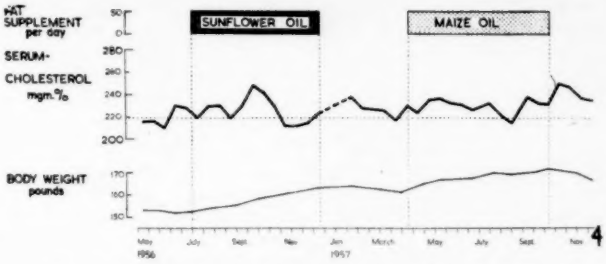

Fig. 4. Subject 10. Neither sunflower-seed-oil nor maize-oil supplements produced a significant change in the serum-cholesterol recorded as in Fig. 2.

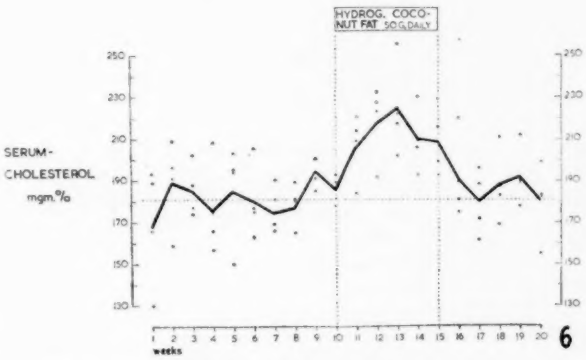

Fig. 6. The weekly changes in the serum cholesterol of subjects 16-19 are recorded. The continuous line represents the mean level for these 4 men. Note that during the hydrogenated-coconut-fat-supplement period, all the serum-cholesterol readings were above the mean level of the first control period.

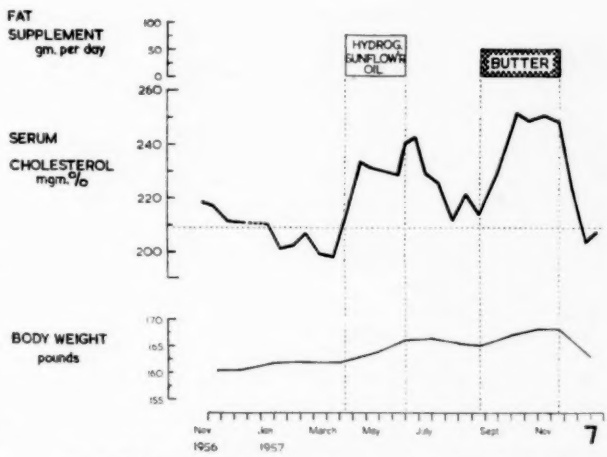

Fig. 7. Subject 20. The increase in serum-cholesterol level produced by a supplement of 75 g. of hydrogenated sunflower-seed oil (iodine value 74) is less than that produced by 50 g. of butter (iodine value 42-46) serum cholesterol recorded as in Fig. 2.

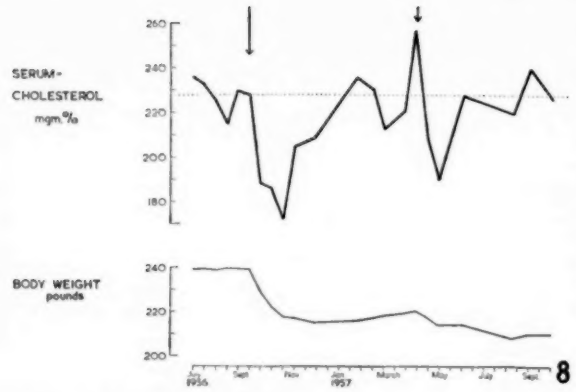

Fig. 8. Subject 21. The arrow indicates when large reductions in daily caloric intake were instituted. These reductions produced sustained decreases in body weight, but only a temporary fall in the serum-cholesterol level. Serum cholesterol recorded as in Fig. 2.

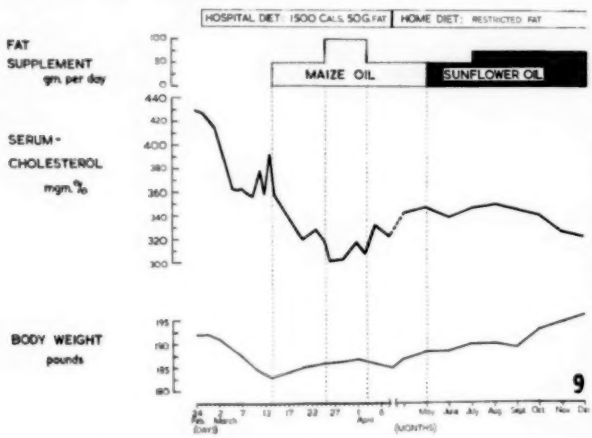

Fig. 9. A case of idiopathic hypercholesterolaemia with xanthomatosis, in a post-menopausal female. The low-calorie, low-fat diet reduced the patient's weight but the decrease in serum-cholesterol level was not maintained. Supplements of maize oil and sunflower-seed oil reduced the serum-cholesterol level and this reduction was maintained despite the weight gain and the resumption of her home diet. (Single serum-cholesterol levels are recorded while on the hospital diet; on the home diet, the serum-cholesterol levels are recorded monthly, each point on the graph representing the mean of 3-4 readings.)

end of the 64 weeks of observation the serum cholesterol was almost exactly at its control level of 218 mg.%.

It will be seen from the data in Tables IV, V and VII that there is no constant relationship between the change in weight during the fat-supplement period and the change in the serum-cholesterol level. Subject 2 (Fig. 1), who had the greatest fall in serum-cholesterol level (87 mg.%), gained the most weight (15 lb.). Similarly, subject 15 gained 10 lb. during the 6 weeks in which he consumed sunflower seeds, while his serum-cholesterol level was substantially decreased (Fig. 5). The dissociation between change in weight and change in serum-cholesterol level is clearly seen in subject 7 (Fig. 2): during the sunflower-seed oil period the subject lost weight, while his serum-cholesterol level fell. During the maize-oil period, the fall in serum-cholesterol level was accompanied by a gain in weight.

Fig. 9 illustrates the observations made in an overweight female subject with idiopathic hypercholesterolaemia. The low-calorie, low-fat diet produced rapid loss of weight and a fall in the serum-cholesterol level which was not sustained. Maize-oil supplements produced a marked fall in the serum-cholesterol level while the subject gained weight. Further unsaturated-fat supplements maintained a reduced serum-cholesterol level despite a more liberal home diet; the body weight, however, returned to its former level.

DISCUSSION

In 1937, Sperry[13] stated that 'in most, if not all, persons in health the concentration of cholesterol in the blood serum is maintained at a constitutional level which is characteristic for the individual and from which large deviations do not ordinarily occur'. Sperry arrived at this conclusion after a study of the changes in the serum-cholesterol level in 25 men and women who, like our subjects, were continuing with their customary activity and diets. In each subject at least 2 and usually 3 estimations of the serum cholesterol were made, at intervals varying from 2 weeks to 28 months. The intra-individual ranges in this group varied from 0 to 49 mg.% with a mean of 20 mg.%. The average standard deviation was 12·1 mg.%.

In our series a comparison of the individual mean serum-cholesterol levels in the two control periods (Tables IV and VI) confirms that each individual has a 'characteristic' serum-cholesterol level which under normal living conditions is fairly constant. But when repeated estimations are made in the same person at frequent intervals and under the same circumstances, marked fluctuations occur about this 'characteristic' level. The data in Table I (summarized in Table II) show that when many readings of the serum cholesterol are made, far greater fluctuations occur than Sperry noted with his comparatively few data. Our findings are best stated in terms of the pooled standard deviation of 14·7 mg.%, which indicates that, when repeated estimations of an 'average' subject's serum cholesterol are made, 95% of the values obtained will be within 29·4 mg.% of his mean level.

Similar data have been reported by Peters and Man.[14] They studied 17 normal men and women but in only 7 of these were 5 or more readings made; in these, the intra-individual ranges varied from 25 to 123 mg.% with an average of 52 mg.%.

Several other studies testify to the intra-individual variability of the serum-cholesterol level. None of these is directly comparable with our own; usually too few readings of the serum cholesterol were made, sometimes with an unacceptable analytical technique, and in most cases the subjects were in hospital on standardized diets. Even under the latter circumstances marked fluctuations may occur. Thus, Hatch *et al.*[15] made repeated estimations of the serum-cholesterol level in 48 hypertensive subjects during a 6-week period in hospital on a controlled diet (calories 2,200, fat 85 g.). The intra-individual range averaged 47 mg.%, which is remarkably close to our figure of 45 mg.% for normotensive subjects on free diets.

Steiner and Domanski[16] have stated that in cases of coronary heart disease far greater fluctuations in the serum-cholesterol level occur than in controls. In their 15 cases of coronary heart disease, who were apparently ambulant and on ordinary diets, an average of 38 estimations of the serum cholesterol were made over periods varying from 2 to 26 months. The mean level for this group was 355 mg.%, the intra-individual range averaged 99 mg.%, and the individual standard deviation averaged 24·8 mg.%. In a control group, these authors found a mean level of 255 mg.%, with an intra-individual range averaging 32 mg.% and an average individual standard deviation of 8·7 mg.%. The control group, however, included cases of peptic ulcer, diabetes mellitus and others on controlled diets in hospital[8] and cannot be compared with the 'coronary' group. In our series, among the few cases of coronary heart disease only subject 14 showed an intra-individual fluctuation which was substantially greater than the mean for the whole group.

It is clear, therefore, that several readings of an individual's serum cholesterol should be made before deciding whether his level is above, below, or within the average limits for his age, sex and race. Serial determinations are also necessary in studying the effect of dietary or other factors on the serum-cholesterol level. In this respect, the 'internally controlled' trial with base-line observations both before and after the experimental period is particularly valuable. If such a procedure were more generally adopted much of the present confusion and contradiction in cholesterol research might be avoided.

FACTORS INFLUENCING THE SERUM-CHOLESTEROL LEVEL

Much of the present interest in cholesterol arises out of its occurrence in atheromatous lesions and the possibility that there may be a relationship between elevated serum-cholesterol levels and coronary heart disease. Cholesterol, however, is present in all animal tissues and it has considerable physiological, pathological and clinical importance. It is chemically related to several biologically significant substances; these include the hormones, progesterone, aldosterone and hydrocortisone; vitamin D; the bile acids; and the benzpyrene group of carcinogenic hydrocarbons. It is an important physiological constituent of myelin and of the red-cell membrane. Pathologically, it is prominent in gall-stones, in xanthomata, and in some chronic granulomatous lesions. Thus, there are many incentives for studying the factors which determine the characteristic level of an individual's serum cholesterol and the deviations which occur from it. The already voluminous literature on the subject is being rapidly expanded. This is a suitable time, therefore, to pause and to assess the present status of our knowledge of these factors.

A. ENDOGENOUS FACTORS

1. *Genetic*

Although the hereditary influences which are so important in cases of hypercholesterolaemia have been very fully studied,[17, 18] their role in determining the serum-cholesterol level in the general population is not yet known. The serum cholesterol is affected by so many environmental factors that the clear separation of the genetic influence from 'family habits' in related persons is extremely difficult. On the other hand, some differences in serum-cholesterol level which at first sight seem to be of environmental origin may in fact be genetically conditioned (e.g. the differences between smokers and non-smokers—see below). Similarly, a genetic factor may account for the variability of individual responses to the same environmental agent, e.g. the failure in subject 10 of both sunflower-seed-oil and maize-oil supplements to decrease the serum-cholesterol level.

An attempt at assessing the importance of genetic factors was made by Gildea *et al.* in 1936;[19] they found that in 12 men of pyknic habitus the mean serum-cholesterol level was 230 mg.%; in 18 leptosomic men the corresponding value was 168 mg.% and in 8 men of intermediate body build it was 203 mg.%. Unfortunately, the sample studied was small and there is no indication that these authors age-matched the groups. More recently, however, in 97 young men with coronary heart disease and in an age-matched control series, Gertler and White[20] found that the ectomorphs (roughly corresponding to the leptosomic habitus) had substantially lower serum-cholesterol levels than the endomorphs and mesomorphs.

2. *Age*

It is generally accepted that the serum-cholesterol level increases with age, but opinions vary about the age when the peak level is reached. For men, it has been variously put at 33 years,[21] 45 years,[22] and 55 years.[23] An increasing serum-cholesterol level is not an inevitable manifestation of the aging process. In Johannesburg, Bersohn and Wayburne[24] found that while European and Bantu babies at birth had similar serum levels (mean of 75 mg.% and 72 mg.% respectively), the European mothers had much higher levels than the Bantu mothers (means of 258 mg.% and 190 mg.% respectively). Furthermore, Pomeranze *et al.*[25] have recently shown that babies fed with an artificial soy-milk formula do not develop the rapid increase in serum-cholesterol level which usually occurs in the first few months of life. Clearly then environmental and genetic factors may be partly responsible for the age-increase in the serum-cholesterol level. The annual increment in an individual's serum cholesterol, however, is small, and is not important in relation to the week-to-week or month-to-month fluctuations.

3. *Sex*

The serum-cholesterol level of men or women may be lowered by the administration of oestrogens.[26, 27] In women, cyclical fluctuations of circulating-cholesterol level have been correlated with fluctuating oestrogenic activity.[28] Thus in 12 healthy young women marked falls in the plasma-cholesterol level occurred at the time of ovulation and just before menstruation, i.e. at the peaks of oestrogenic activity. In 6 healthy men no cyclical changes were observed. It is presumably the activity of oestrogenic hormone which accounts for the fact that women often have lower serum-cholesterol levels than men during the reproductive years of their lives.[21, 29]

B. EXOGENOUS FACTORS

1. *Season*

In 1924, Currie[30] reported that in Glasgow the plasma cholesterol of normal individuals varied with the season, the highest levels occurring in summer (mean, 280 mg.%) and the lowest in winter (mean, 110 mg.%). He suggested that these changes might be due to seasonal variations in the

food supply or to a stimulating effect of sunshine on endogenous cholesterol synthesis. Currie did not explain how he obtained his data and it appears that different groups of subjects were analysed in the different seasons. Furthermore, his technique for measuring the plasma cholesterol is not acceptable. In 1932 in Canada, McEachern and Gilmour[31] refuted Currie's findings, but their data too are quite inadequate. It must be concluded that the effect of seasonal changes on the serum-cholesterol level are unknown.

2. *Exercise*

The low serum-cholesterol levels of underprivileged races have been attributed by Mann *et al.*[32] to the greater physical activity of these peoples. In the Cape Peninsula inter-racial survey,[33] it was found that the Bantu heavy labourers had lower serum-cholesterol levels than the Bantu light workers; in the European and Cape Coloured groups, however, there was no relationship at all between degree of physical activity and the serum-cholesterol level. In a wider survey, including data from Italy, Sweden, the USA and South Africa, Keys *et al.*[34] concluded that the activity of work played only a minor role in regulating the serum-cholesterol level.

Nevertheless, other lines of investigation have indicated the importance of exercise. In their classical studies of the extraneous factors influencing the serum-cholesterol level, Groen *et al.*[3] found that in their subjects increased physical activity often had a marked lowering effect. Taylor *et al.*[35] demonstrated the effect of exercise in 9 healthy young men; when they increased their fat intake by 46 g. daily and at the same time increased their calorie expenditure by walking on a treadmill for 2 hours, no increase in serum cholesterol occurred. Presumably the increased exercise prevented the anticipated rise in the serum-cholesterol level, but the value of the experiment would have been enhanced had the effect of the fat increment also been studied in the same subjects without exercise.

The evidence, then, is fragmentary and not conclusive but it is sufficient to suggest that varying activity may partly account for otherwise unexplained serum-cholesterol fluctuations.

3. *Smoking*

Gofman *et al.*[36] have found higher levels of serum cholesterol in those smoking 20 or more cigarettes daily than in non-smokers. The differences, however, were not striking; they were maximal in men aged 20-29, among whom the serum cholesterol of the smokers averaged 226·4 mg.% as opposed to 205·2 among the non-smokers. Bronte-Stewart noted a similar relationship among the European and Cape Coloured men under 40 years of age in the Cape Peninsula.[37] He suggested that the heavy smoker dulls his palate and therefore seeks out spicier and more savoury foods; the latter are rich in fat and it is this factor which increases the serum-cholesterol level rather than smoking *per se*.[38] This suggestion is interesting, but the evidence relating smoking and the serum-cholesterol level is scanty and requires further study.

4. *Physical Stress*

Acute physical stress has been shown to decrease the serum-cholesterol level. Thus Kyle *et al.*,[39] in 10 cases, observed a mean fall of 16% 8-72 hours after a variety of major surgical operations. Similarly, Biorck *et al.*[40] have reported that the serum-cholesterol level may fall after acute cardiac infarction. In some of their patients it appears that this fall was transient, but in most cases the studies were incomplete. Neither of these two groups of authors make mention of their patients' food consumption and it is possible that the falls in the serum-cholesterol level may have been partly due to dietary restriction in the early post-operative or post-infarction period. McQuarrie and Stoesser[41] studied the effect of acute infections in 27 children. They found that at the height of the illness the serum cholesterol was low in comparison with its level on the 8-9th day of convalescence; in general, the serum-cholesterol level varied inversely with the white blood count. Some of their patients were on a constant diet throughout the period of investigation, and it was shown that in these the serum-cholesterol changes were independent of the food intake. In 9 children with afebrile disorders, the production of artificial fever with TAB etc. was without effect on the serum cholesterol, indicating that fever as such is not responsible for the low levels encountered in infections.

In adult subjects on various dietary regimes, Groen *et al.*[3] found that reductions in the serum-cholesterol level occurred with upper-respiratory-tract infections and with gastro-intestinal disorders. We have noted similar effects; in Fig. 10 some examples are shown of the changes in serum cholesterol apparently resulting from accompanying influenza,

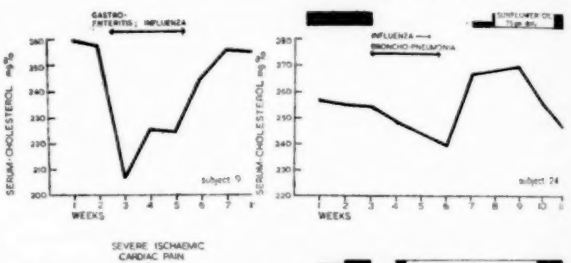

Fig. 10. The week-to-week changes in the serum-cholesterol level accompanying infection, bowel disorders and coronary insufficiency.

pneumonia, gastro-enteritis and coronary insufficiency in subjects on their usual home diets with and without fat supplements. It must be emphasized, however, that both in our experience and from a perusal of the records published by Groen *et al.* it is not always possible to distinguish the changes due to physical stress from apparently 'spontaneous' fluctuations in the serum-cholesterol level.

The mechanism of these changes is not known. Stoesser and McQuarrie[42] in 1935 suggested that cholesterol combines with bacterial toxins and its circulating level falls. More recently, the role of the pituitary-adrenal axis has been invoked. In normal subjects ACTH produces a fall in the

serum-cholesterol level.[43] It is postulated that stress increases the production of ACTH, which in turn stimulates adrenocortical activity; thus the conversion of cholesterol to adrenal hormone is enhanced and the level of circulating cholesterol falls. It may be noted that in normal persons cortisone, which does not promote cholesterol-corticosteroid turn-over, has little effect on the serum-cholesterol level.[43] Studies of the action of ACTH and cortisone on the blood lipids in normal men are scanty and further investigation is necessary.

5. *Emotional Stress*

The quantitative study of emotional stress is almost impossible and an assessment of its effect on the serum-cholesterol level is fraught with difficulty. Nevertheless, Groen *et al.*[3] gained the impression that domestic disharmony and business difficulties increased the serum-cholesterol level of some of their subjects. Very recently, Hammerstein *et al.*[44] have studied 12 men who had survived cardiac infarction. Weekly estimates of the serum-cholesterol level were made under conditions which apparently resembled those of our study except that the diets were more standardized. They report that 'on 20 occasions the serum cholesterol rose higher than the mean value for that individual by more than 15%. It was striking that 19 of the 20 occasions of high cholesterol corresponded with periods that had been separately judged as particularly stressful for the individuals concerned'. A similar result has been reported by Rosenman and Friedman,[45] who measured the serum cholesterol of 42 accountants twice weekly during the first half of 1957. They found that, with the increased pressure of work preceding the business 'dead-line' periods, the serum-cholesterol level was substantially higher than during less turbulent times. Both these investigations have only been reported in abstract and their detailed publication is awaited with interest.

6. *Diet*

We have recently reviewed the role of various dietetic factors in determining the serum-cholesterol level[46] and this discussion will be restricted to those aspects which are relevant to the present investigation.

(*a*) *Caloric Balance.* Walker *et al.*[47] have stated that 'caloric balance appears to play a major role in controlling . . . serum-lipid levels'. In their study of 39 subjects, however, weight reduction had little significant effect on the serum-cholesterol level. On a diet containing 1,250 calories, of which 36% was derived from fat, their subjects lost on the average 19 lb. in 106 days (i.e. about 1·6 lb. per week). During this period, the mean reduction in the serum-cholesterol level for the group was 17 mg.%, which is not statistically significant. In fact, those subjects who lost most weight actually showed an increase in the serum-cholesterol level.

Several other studies testify to the inconsistent effects of weight reduction. Poindexter and Bruger,[48] using very low-calorie diets (600-885 calories, with about 30% from fat) produced substantial reductions in weight but the serum-cholesterol level increased in some subjects and decreased in others. Both Young *et al.*[49] and Moore *et al.*[50] in studies on overweight women found that reducing diets (1,400 to 1,500 calories with 48-50% from fat) generally raised the serum cholesterol while the weight fell.

The amount of fat in the reducing diet is important in determining its effect on the serum-cholesterol level. Thus, Anderson *et al.*,[51] using isocaloric reducing diets (1,200 calories), have shown that with 18% fat-calories, the serum-cholesterol level is lower than with 58% fat-calories.

Passing from reducing diets, we need to consider the effects of chronic malnutrition. Keys *et al.*[52] in their monumental work *The Biology of Human Starvation* have summarized the literature on the effects of complete and partial starvation on the blood lipids in man, and draw attention to the inadequacy of the data and the inconsistency of the results. In their own experiment on 36 conscientious objectors who subsisted on semi-starvation rations for 6 months, the fall in the serum-cholesterol level, although statistically significant, was quite small. The mean level on the control diet (total calories 3,492, fat-calories 32%) was 169 mg.% and by the end of the semi-starvation regime (total calories 1,570, fat-calories 17%) it had fallen to 152 mg.%. This fall in the serum-cholesterol level was accompanied by an average loss of 18·5% of body weight.

Our colleagues Schendel and Hansen[53] have recently reviewed the literature and reported their own observations on the changes in the serum cholesterol which occur in protein malnutrition of infants (kwashiorkor). During the acute stage, the serum-cholesterol level is very low (mean, 93 mg.%); in those cases in which a satisfactory initiation of cure accompanies the administration of a fat-free diet, it rises promptly to normal levels (mean, 179 mg.%). Most cases of kwashiorkor, however, are complicated by respiratory or intestinal infection, and this may be at least partly responsible for the low serum-cholesterol levels.

Finally, we note that the effect of caloric increase has been inadequately studied. Walker *et al.*[47] have claimed that in two cases the supplementing of the basal diet with 2,000 calories derived from carbohydrate increased the serum-cholesterol level. From the data which they present, however, we are unable to draw the same conclusion. Our own limited investigations (unpublished) have shown that the increase in the serum-cholesterol level which accompanied large carbohydrate supplements is small and slow when compared with calorically equal or lesser supplements of saturated fat.

(*b*) *Low-fat Diets.* Low-fat diets are often recommended for decreasing the serum-cholesterol level and, while such diets are generally effective in this respect, it must be realized that very severe fat restriction is necessary to produce an adequate response. For example, Anderson and Keys[54] achieved a fall of only 21 mg.% by changing the fat content of the diet from 140 to 70 g. (i.e. from 37% to 18·5% fat-calories). In two large series of hypertensive cases treated with the notorious rice diet (which is almost fat-free), Kempner[55] and Starke[56] reported decreases in the serum-cholesterol level of 57 mg.% and 71 mg.% respectively. It must be noted that in these studies there was no control period and only single estimations of the serum cholesterol were made before and after institution of the diet. On the other hand, Hatch *et al.*[15] have conducted a careful investigation into this type of diet; several estimations of the serum-cholesterol level were made both during a control period and during the various dietary regimes, all of which were carried out in hypertensive subjects in hospital. The control diet (2,200 calories) contained 85 g. of fat (35% fat-calories). Changing to diets containing 55 and 20-40 g. of fat respectively produced insignificant falls in the serum-cholesterol level. Changing to the rice diet (3 g. of fat) for 4-20 weeks produced a mean

fall of 33 mg.% in a group of 44 patients; i.e. a fall which is almost the same as that produced in our 10 subjects simply by supplementing their regular diets with 50 g. of unsaturated fat. Most patients will rebel against the continued use of very low-fat diets and it is unlikely that they will be widely used in practice for reducing high-serum-cholesterol levels.

(*c*) *Unsaturated Fats.* The present investigation has shown that the changes produced by unsaturated fats in acute metabolic experiments and with artificial diets can be reproduced under normal living conditions by feeding the fats as supplements to the diet. It also appears that the effect of these fats can be maintained for as long as they are consumed and that their activity is independent of changes in body weight.

The sustained reduction in the serum-cholesterol level is consistent with the epidemiological evidence. The association in the Eskimo of relatively low serum-cholesterol levels with high intakes of unsaturated marine fats has been repeatedly observed.[57] In Yugoslavia, Brozek *et al.*[58] compared two populations; those living on the mainland in the North consume large amounts of animal fat and have significantly higher serum-cholesterol levels (238 mg.%) than their compatriots living on islands off the Adriatic coast (198 mg.%), who have a quantitatively similar fat intake which is, however, almost entirely olive oil. Similarly, in a survey amongst clothing workers in New York, Epstein *et al.*[59] found that Jews had higher serum-cholesterol levels (248 mg.%) than Italians (226 mg.%); the total fat intake was the same for both groups, but 32% of the Italians' fat intake was from vegetable sources while the Jews obtained only 20% of their fat from this source. Finally, it will be recalled that vegetarians may consume substantial amounts of fats most of which are unsaturated but they maintain relatively low serum-cholesterol levels.[60-62]

The routine use of unsaturated-fat supplements as a practical measure for lowering serum-cholesterol levels is probably undesirable. Many individuals will find the consumption of about 4 tablespoonsful of oil daily irksome or unpleasant. Moreover, there may be a marked gain in weight. In practice, it is likely that the most satisfactory cholesterol-decreasing regime will be one in which the foods containing saturated fats are moderately restricted and partly replaced by foods rich in unsaturated fats.[46]

It is, however, of interest in this connection that several of our subjects did not gain weight during the fat-supplement periods and the total weight change for the groups was far less than was expected from a caloric increment of 450 daily. There was no evidence of malabsorption in any of these subjects, so it is likely that they must unwittingly have been restricting their food intake. This can probably be attributed to the well-known 'satiety effect' of dietary fat, but an internal metabolic effect of the fat can at present not be excluded.

SUMMARY

1. Repeated estimations of the serum-cholesterol level have been made in 30 men during an observation period averaging 13 weeks. During this period the men continued with their customary activities and consumed their usual home diets. In these men, it was found that while there appears to be a characteristic level of serum cholesterol for the individual, there may be marked fluctuations around this level from week to week. The causes of these fluctuations are not always apparent.

2. In 10 of these men, the long-term effects of a dietary supplement of unsaturated fat have been investigated. In 8 of them a significant decrease in the serum-cholesterol level was produced; the mean decrease for the whole group was 34 mg.%. On withdrawing the unsaturated-fat supplement, the serum-cholesterol usually returned to its former level. In 5 of these men, a second trial, with a different unsaturated fat, produced a similar effect.

3. In another 5 men it was shown that, under similar circumstances, saturated-fat supplements raised the serum cholesterol significantly.

4. The effects of the fat supplements were independent of changes in body weight.

5. The endogenous and exogenous factors which regulate the serum-cholesterol level are reviewed. It is concluded that the most practical cholesterol-decreasing regime is one in which saturated dietary fats are moderately decreased and partly replaced by unsaturated fats.

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ANGIOMA OF A MALE BREAST WITH MALIGNANT CHARACTERISTICS

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This case is presented because of its great rarity and the scant attention the condition receives in the literature. Only casual references to angioma of the breast are made in some standard works,[1, 2] whilst others do not mention it at all. This fact is rather surprising, since Ewing[3] described it in his work in 1919. The first reference to it was made by Bormann[4] in 1907. In all 18 such cases have been described previously. These were all in females. There are thus sufficient cases on record for it to be regarded as a clinical entity, and therefore to put on their guard clinicians and pathologists alike in dealing with a similar case, rare as it may be.

CASE HISTORY

The patient was a young African male aged 17 years, in good general health, mentally and physically. He gave a history that 'ever since he can remember' the chest wall had been slightly more prominent on the left side than the right. The left breast began to increase in size more noticeably in the last 2 years, i.e. since about puberty.

It had reached the size of a cricket ball when, 2 weeks before admission, the left breast began to swell rapidly and caused pain, until it reached the size shown in Figs. 1 and 2. There is no known history of trauma. At this juncture a doctor was consulted. A diagnosis of breast abscess was made and the swelling was incised. The result was alarming. A brisk haemorrhage ensued, which was controlled with the assistance of a fibrin foam preparation and gauze dressings, but oozing persisted for a few days.

During this interval the patient was transferred to hospital, 70 miles away. On admission his condition was very good and, apart from the discomfort of the tumour, he was quite happy and comfortable. Temperature, pulse and blood pressures, etc., were normal and no other abnormality could be found in any of the systems.

The tumour was almost circular and measured 8 inches across its diameter. It closely resembled a female breast, as may be seen in Fig. 1, except for a rather small nipple. The mass was soft and fluctuant, but tense in some areas and softer in others. It was well demarcated from the surrounding chest wall but was not mobile, being fixed to the underlying pectoral muscle. It was non-tender, although apparently it had been tender before incision, and the surface temperature was higher than that of the surrounding skin. The overlying skin was normal over the firmer areas, but thin and shiny where the tumour was softer. Redness cannot be observed clearly in such dark-skinned individuals, but the skin over the tumour was decidely darker than the rest of the body. The wound of the first incision, about $\frac{1}{2}$ inch long, was closed and dry, and filled with black clotted blood.

A tender axillary gland, about the size of an almond, was palpable on the left side. It was fairly freely mobile and rubbery-firm. No other adenopathy was present.

A haemic bruit, rather faint and muffled, could be heard on auscultation of the tumour.

Radiology of the skeletal system showed no abnormality; nor did similar investigation of the chest and abdomen.

The diagnosis of a vascular tumour was fairly obvious. In view of the rapid increase in size, and the pain, it was thought that malignant change was present, and angiosarcoma was diagnosed. The treatment therefore decided upon was removal of the breast, which was carried out by radical mastectomy. The wound was closed completely and it healed, somewhat surprisingly, uneventfully.

Figs. 1 *and* 2.

There was no disability and no untoward sequelae occurred in the subsequent 6 months. Regrettably, the patient was not seen again—the usual follow-up difficulty with such patients.

Macroscopically the tumour extended to muscle, and consisted largely of numerous blood-filled spaces of varying sizes and shapes, the more superficial being the larger. Some areas of the tumour were covered by skin and fascia, others only by skin, which was adherent. Scattered areas of fat and fibrous tissue intermingled with these 'blood-lakes' which were not delimited by any form of capsule.

Histologically the vascular spaces were lined by endothelium, which was poor in parts and tended to be absent where covered by skin only. The mesenchymal tissue was richly vascular with capillaries and veins and vessels with varying development of muscle coats. Some irregular perivascular cells and scattered leucocytes were evident. There was no evidence of infiltration, mitosis or other sign of malignancy.

Section of the gland showed inflammatory change only.

DISCUSSION

The first reaction to be expected from this case history is that the tumour, after all, was not malignant, as there was no evidence of infiltration, no glandular involvement, and no histological evidence of malignancy.

It would be appropriate at this juncture to point out the variety of nomenclature that has been attached to this tumour, as is so often the case with any little understood condition. It has been called angiosarcoma, haemangioblastoma, malignant angioma or haemangio-endothelioma, etc., and even benign metastasizing angioma, which, of course, is a classic contradiction of terms, but illustrates the difficulties in histological diagnosis.

Let it be said at once that errors of microscopic diagnosis are very frequent in this condition. McClanachen and Hogg,[5] in their review of 6 cases, state that the disarmingly innocent histological appearance of angiosarcoma (haemangioblastoma) is most misleading, and that the tumour is in fact malignant. This view is similarly held by Patrick, Jarvie and Miln,[6] who recently described 3 more cases. The experience of most of the writers[7-10] who have recorded cases has been similar.

Several aspects of the present case closely resemble those features which are common to all the malignant vascular tumours of the breast that have been described. The patients are nearly always young, in their 2nd or 3rd decade, and the history is recent, being a matter of months. Trauma appears to have played some part.

In all cases the primary growth is massive, and has attained its size in a few months. There is invariably overlying skin discolouration. As in this case, the tumour consists of a large friable haemorrhagic mass varying in appearance in different parts, both macroscopically and microscopically. There is never any involvement of axillary nodes, and no evidence of encapsulation.

Further important negative points are the absence of discharge from the nipple, retraction of the skin or oedema.

McClanachen and Hogg[5] hint that benign angiomas are never of bulky size but are always small and discrete, and the walls of their vessels are thicker. One readily admits that histologically angiosarcoma in some areas is of this nature, but one feels that serial sections will almost always reveal the features of malignancy.

Histologically there was no confirmation of malignancy in the present case. Patrick, Jarvie and Miln[6] emphasize the difficulty in distinguishing malignant cells in these tumours, and quote several instances where they were in fact not found, but nevertheless the patients succumbed from metastases. McClanachen and Hogg[5] confirm this by their assertions that the histology is deceptively benign to those unfamiliar with the condition. In no fewer than half the cases recorded malignant characteristics were not found histologically, but all the cases died from secondary spread in an average of just over 2 years; hence the erroneous term benign metastasing angioma.

The tumour in question seemed obviously a cavernous haemangioma of developmental origin arising in the left breast. The malformation increased in size *pari passu* with the host until, probably owing to inadvertant minor trauma and inflammatory change, it rapidly became larger. It was situated in an exposed region, which in a young African male is particularly prone to repeated minor trauma. It would be feasible that this and low-grade infection should give rise to a rapid increase in size, even if the benign nature of the mass were accepted without question. This explanation would be even more acceptable concerning the events in a malignant mass in which trauma, causing interstitial haemorrhage in a friable mass, added to the size of an already rapidly growing tumour.

The combination of the above evidence, one feels, must be accepted as strong argument in favour of malignancy in this case.

No close relationship with the pectoral muscle was made out in the way of bundles of muscle fibres between the endothelial lined spaces. This discounts the possibility of haemangioma of muscle, also a rarity, but perhaps more generally recognized.

The ultimate outcome in this case is not known, and it is indeed most unfortunate that adequate follow-up was not possible. Had it been, the diagnosis of malignancy would doubtless have been confirmed.

A common cause of death is haemorrhage from a secondary deposit. Haemoptyses are frequent. The average interval between diagnosis and death is just over 2 years, often less than 1 year.

Aetiology

A brief mention of aetiology may be made. Other reported cases give no indication of the previous existence of a congenital malformation. In the female the normal contours of the breast would easily obscure this; a small unnoticed mass could rapidly enlarge and become prominent, and perhaps even resemble a subcutaneous haematoma. The occurrence of this growth in a male breast provided a means of closer observation, and the existence from birth of a mass seems fairly certain.

An interesting suggestion is the hypothesis of multifocal angiomatous malformations, simulating metastases. There is little evidence to support this, apart from the constant post-mortem findings. Local recurrence and pulmonary metastases are the most frequent. Other sites of spread are to bone and viscera.

Differential Diagnosis

The diagnosis should present less difficulty once a case has been seen or the possibility of the condition realized. It should be differentiated from other forms of sarcoma, adenocarcinoma, giant fibro-adenoma, cystosarcoma phyllodes, haematoma, lipoma, unilateral hypertrophy, infected cysts, and tumours of the chest wall.

Treatment

A satisfactory method of treatment is not known. This may be due, in part, to the delay in diagnosis and in recognition of the malignancy of the tumour. In the cases reviewed, all known forms and combinations of treatment were carried out with apparently little difference in the end-result. The methods used included both local and radical excision of the breast, with or without radiotherapy. One case was treated with pre-operative radiotherapy followed by radical excision.

Radical mastectomy was performed in the present case, but the outcome is not known. As in the treatment of malignant disease of the breast in general, the question of local or radical operation is still debated. The constant absence of axillary glandular involvement would favour local removal. However, unless one can be sure of removing the mass from the pectoral fascia and muscle, it is probably best to remove this structure. By and large, the treatment of choice at present is probably simple mastectomy followed by radiotherapy. The use of roentgen rays should always follow either surgical procedure. The response of secondary deposits to radiotherapy is disappointing.

SUMMARY

A case of angioma of the breast (in a male) is presented. This rare tumour and its characteristics are described, and discussed.

A case is made for the malignancy of the case presented. The importance of serial section in revealing malignant cells is stressed.

Brief mention is made of the aetiology, differential diagnosis and treatment.

My thanks are due to Dr. E. Holland, formerly Medical Superintendent of the Eshowe Hospital, Zululand, for permission to treat the case and publish this report. I am indebted also to Mr. Stead, formerly of Eshowe, for the photographs.

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MEDICAL CULPABILITY *

B. CROWHURST ARCHER, M.D.

Durban

In a criminal case when the plea of insanity is raised by the defence, most medical men find particular difficulty over the criteria of irresponsibility laid down in the McNaughton rules.

They feel that these rules savour of the outmoded academic doctrine of the mental faculties—according to which mind was thought to be divided into a series of independent compartments, the cognitive faculty being one of the larger subdivisions. Medicine has come to recognise 'mind' as a whole and that however partial a mental disorder may appear the whole mind is affected. The Doctor does not accept a purely intellectual conception of responsibility, for even if intellect as intellect were unimpaired, emotion could alter its effect on conduct. Conversely, intellectual defect produces deficient emotional control.

In other words, the legal concept of mind, as Peskin (1954) has pointed out, is based on the ecclesiastical and philosophical concept that man possesses a free will, is capable of deliberately choosing between good and evil, and is therefore accounted fully responsible for his choice of action. On the other hand, the study and practice of psychiatry incline its adherents more and more to the doctrine of Determinism, i.e. that behaviour is largely, if not entirely, determined by factors which are really beyond voluntary control. The 'will' is dictated to by unconscious strifes and motives which in turn owe their origin to a combination of circumstances—heredity, constitutional and environmental.

There is therefore no allowance in law for such well-known mental states as the disconnection between thought, feeling and action and the absence of a goal idea resulting in impulsive action in cases of schizophrenia and post-hypnotic and epileptic automatism, the overpowering depression of affective disorders which cause a parent to murder the children whom he loves, knowing full well that it is morally wrong to kill, to say nothing of the behaviour disorders that may follow encephalitis lethargica.

It is only fair to remind ourselves that the McNaughton case did not come before the House of Lords in its judicial capacity, and the well-known questions of the Judges and the answer of the Lords only referred to the effect of insane ignorance and insane delusions, and that the Court of Criminal Appeal, when refusing to accept a plea of insanity, which the jury had disregarded at the trial, frequently calls attention to the fact that the Secretary of State has special powers to enable him to order a medical enquiry concerning the mental condition of appellants convicted of murder.

I find myself in agreement with those who believe that if a medical formula of criminal responsibility were introduced we might be called upon to adhere rigidly to its specifications, with resulting hardship to offenders and embarassment to psychiatrists. The immediate need is not a reform in the law regarding criminal responsibility but an improvement in the evidence we give as forensic psychiatrists.

MEDICAL CULPABILITY

Criminal Courts are courts of law, and not courts of morals, and the psychiatrist may well leave the problem of criminal responsibility to the lawyers and direct his attention to the concept of 'medical culpability'.

East (1949) has expressed the opinion that psychiatry has advanced sufficiently to justify the acceptance of the principle of modified culpability in convicted offenders suffering from a

* A paper read in a symposium on 'Criminal Responsibility and the Psychopath' at the South African Medical Congress, Durban, September 1957.

recognised minor mental abnormality, if the degree of blameworthiness lies somewhere between that attached to the unlawful act of a normal person and one who is insane according to the law. For this purpose a clear mental classification of offenders would be necessary, separating the normal, the sub-normal, the mentally defective, the psychopathic, the psychoneurotic and the psychotic groups from one another.

The mentally normal group of offenders comprises at least 80% of receptions. Statistics for Great Britain show that the proportion of mentally defectives is about 0·5% and of the insane 1·0%. Research is necessary before estimates can be made of the proportion of offenders who are sub-normal, psychopathic personalities, and psychoneurotics.

The criminal psychopathic personalities include the unstable drifter, the sexually perverse, the cold and emotionally callous, and the 'epileptoid'; as well as the epileptic with psychopathic trends and psychopathy resulting from cerebral injury and other organic diseases of the brain.

Henderson (1950) said of the psychopath that he believed that such cases should be treated not necessarily with greater severity but under more special conditions and for such time as to prevent possible recurrence of the offence. His plea was for an indeterminate sentence until a sense of social responsibility became established. If the attitude of the courts were more in keeping with this opinion the defence of psychopathic personality might understandably become less popular.

R.N.A.H. Cholmondeley Castle

During the war I was Medical Officer-in-Charge of a castle in the North of England used as a Royal Naval Hospital for Neuropsychiatric Disorders. The conditions of admission were that prospective patients had had a reasonably sound personality before entry into the Service and that they were considered by the psychiatrist recommending the case to have a reasonable chance of returning to duty. The methods of treatment and the reason for the successful results obtained are a little outside the scope of our discussion, save to say that the patients were resocialized against a background of service discipline by every modern means of psychiatric treatment. Something, however, may be said about my 'opposite number'—a special camp known as *H.M.S. Standard.*

H.M.S. Standard

The cases drafted to this establishment included men possessing such low morale or such a degree of temperamental instability as to make them unemployable as combatants. They included those ranging from the constitutionally timid to the rank coward and the malingerer—men showing no symptoms that would make them legitimate subjects for survey on purely medical grounds while their release from the Service on any pretext would have had a bad effect on the others. These men were recommended by medical officers, and were returned to their Port Division for examination by the depot psychiatrist, the final decision whether to draft them to the Camp resting with the Commodore of Barracks, who acted as a magistrate.

The men were under ordinary naval discipline, but the routine was sufficiently severe, especially in the earlier stages of treatment, to act as a deterrent to men whose chief object was to avoid arduous service. Men were employed on hard physical work most of the time. Education in the broadest sense and lectures formed part of the routine. Organized games on Saturday afternoon were permitted but solitary recreations were discouraged except on Sunday afternoon, which was mostly devoted to letter writing.

Contrary to expectation at the end of the first 6 months, 25% returned to sea and 25% to shore and harbour service. I merely mention this to show what was done by different methods of rehabilitation.

Belmont Social Rehabilitation Unit

Soon after the war Maxwell Jones (1952) established a Social Rehabilitation Unit at Belmont Hospital in Sussex, England. This Unit consisted of 100 beds, which were reserved for the treatment of character disorders of both sexes. Maxwell Jones's aim was to subject the anti-social individual to a social experience which might lead to some modification of his behaviour by lessening his social tensions and thus help him to gain greater satisfaction from his social relationships.

The patients consisted of the misfits in industry and were admitted from the employment exchanges, but others were referred by psychiatrists and by the Courts. Their stay in hospital varied up to a period of 12 months. It is claimed that in this atmosphere of group endeavour the psychopath develops concern about the disturbance his anti-social behaviour has caused in the community, and that as his feelings of guilt increase he begins to identify himself with the aims of the Unit.

Institute for Criminal Psychopaths

The experiment at present being carried out at the Institute for Criminal Psychopaths at Herstedvester in Denmark is of particular interest in this connection. Under Section xvii of the Danish Criminal Law, patients suffering from mental disorder other than insanity or mental defect may be sent to this Institute on an indeterminate sentence, where their discharge can only be sanctioned by the Court which convicted them.

The routine of this establishment differs from that of *H.M.S. Standard* in that work is not compulsory but luxuries such as cigarettes can only be obtained by voluntary labour. Organized games, entertainment and opportunities for further education are part of the ordinary routine. The ability to adjust himself to the work and social background of the Institute is one of the criteria of the man's fitness for discharge. So far as discipline is concerned, the only mitigation accepted for anti-social behaviour is great emotional stress.

On admission patients are usually over-optimistic, but after a few months this optimism gives way to despair as they begin to realize that they are serving an indeterminate sentence. It is at this juncture that individual psychotherapy is added to the already existing methods of group therapy. An all-out attempt is now made to socialize the individual against the background of the Institute. This background is built up on laws which resemble those that exist in the outside world but which are more logical and just. I cannot help feeling from my own experience that the successful results that have so far been claimed in this experiment—and they are good, about half the cases admitted having been satisfactorily settled in the outside world—are due to the background of the establishment. This background seems to have promoted a high degree of *esprit de corps* amongst the staff, which has in turn been imparted (in some instances unwittingly) to the inmates.

Sturup (1952) has pointed out that difficulties might arise in such an organization because the doctor-patient relationship would be overshadowed by the physician's responsibility to society. But if it is the background of the establishment rather than the individual doctor alone that is responsible for the success of the experiment, then this criticism is not nearly as important as it would first appear.

The director of such an establishment would of course have to be carefully selected. It might be found that the most suitable director was a Physician-Superintendent who had had previous administrative experience in the fighting services, and who had developed to a high degree what General Wavell referred to as 'the art of man mastership'. On the other hand, one could envisage in certain circumstances a kind of joint directorship, consisting of an experienced head of a progressive Borstal Institution and an administrative psychiatrist.

If you doubt the wisdom of this last suggestion, I can remind you of the organization of hospital ships in the Royal Navy Here the Master of the ship and the Surgeon Captain are in joint command. It is true that the Master is master of the ship in every sense of the word, but the Principal Medical Officer has no difficulty, for instance, in requiring the Master to reduce speed in the interest of the sick. So far as human relationships are concerned, hospital ships are renowned throughout the fleet as 'happy ships'.

It is generally agreed that the criminal psychopath is as much out of place in a mental hospital as he is in a prison. A special institution is required for such persons but it is not suggested that in the present state of our knowledge either the criminal psychopath or the homicidal lunatic is likely to be very amenable to treatment, particularly as most forms of therapy require some cooperation from the patient. First offenders and those guilty of less serious crimes are much more likely to respond to treatment.

With the provisions of such an institution and the greater use of the indeterminate sentence, the much-needed research could be carried out. We know that instinct may act with ordinary, diminished or excessive force, or it may be perverse, but so far these variations cannot be accurately measured. It might be shown that perverse aggressive and acquisitive conduct, like perverse sexual conduct, is variable in form and causation, and is based on a special type of personality which to a large extent is unaffected by ordinary penal methods.

In conclusion, it appears that the psychiatrist can best help the Court in determining the medical culpability after the accused has been found guilty and, while it is felt that our profession can offer sound advice in cases of psychosis and neurosis, a great deal more research will have to be done before we can evaluate criminal behaviour beyond the region of mental disease. Expert evidence in these cases should be given by trained psychiatrists and they should take care under examination not to overstate their case and advance theories and hypotheses that have not been generally accepted by the profession. Above all they should never forget when they testify that they themselves and the profession they represent are on trial (Kozol, 1949).

In the present state of our knowledge it can only be said that the more nearly a crime appears to be in the nature of a character defect as distinct from a recognized mental disorder, the more likely is the accused to be responsible for his actions.

For a certain proportion of offenders, the practical measure would be an indeterminate sentence, which would protect society, and the establishment of an Institute for Criminal Psychopaths which, incidentally, would provide the much-needed facilities for research.

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ASSOCIATION NEWS : VERENIGINGSNUUS

EAST RAND BRANCH

The annual general meeting of the East Rand Branch of the Medical Association of South Africa was held at the Boksburg-Benoni Hospital on 23 January 1958. Dr. E. Meltzer presided and 27 members were present.

Secretary's Report. Dr. W. M. Bezuidenhout presented the secretarial report. He stated that the membership had increased during the year from 213 to 225. During the year 11 Branch meetings had been held, with an average attendance of 18, 4 being business meetings and 7 clinical meetings. The attendance at the latter had been disappointing. Dr. A. H. Tonkin addressed a business meeting in August.

The Branch Council had held 12 monthly meetings in addition to meetings with the Southern Transvaal Branch to discuss contract practice matters. Finality had not been reached concerning the Transvaal Clothing Industry Medical Aid Society. The Springs Industrial Benefit Society, the Roodepoort-Maraisburg Non-Scheduled Mines and Industries Benefit Society and other benefit societies had been under review.

The secretary also reported on the social functions, including the Jooste Cup Golf Competition and the Annual Dinner-Dance at the Benoni Country Club. A cocktail party had been held at the Springs Country Club to welcome Dr. and Mrs. Routley. Dr. Routley was president of the Canadian and British Medical Associations and Consultant General to the World Medica Association. Dr. and Mrs. Gould accompanied Dr. and Mrs. Routley on a 3-day visit to the Kruger National Park.

Elections. The Branch Council members for 1958 were as follows: *President* Dr. A. L. Karstaedt. *Vice-president* Dr. A. Gould. *Immediate past-president* Dr. E. Meltzer. *Hon. Secretary-Treasurer* Dr. W. M. Bezuidenhout. *Members of Council:* Dr. G. C. F. van Helsdingen (Germiston etc.), Dr. J. Noll (Boksburg), Dr. J. N. P. Leonard (Benoni), Dr. K. A. Gough (Brakpan), Dr. S. Copans (Springs), Dr. J. Q. Ochse (remaining areas).

At the Federal Council elections, which were held during the year, Dr. E. W. Turton, Dr. M. Segal and Dr. D. E. Mackenzie were elected to represent the Branch on Federal Council. They are *ex officio* members of the Branch Council.

Honorary Members. Dr. E. J. Papenfus was elected and Dr. G. B. Moffatt re-elected honorary member of the Branch for 1958.

Press Liaison Committee. It was agreed to appoint a press liaison committee, which would enable publicity to be obtained on certain subjects without the personal publicity that was involved when individual colleagues gave interviews.

Specialist Regulations. It was agreed to refer to Federal Council recent changes in the Medical Council rules which it was con-

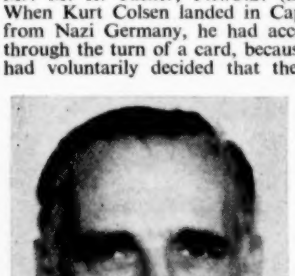
sidered lowered the standard of entry to the Specialist Register.

Induction of President. Dr. Meltzer in inducting Dr. Karstaedt thanked Dr. Bezuidenhout and all Branch Councillors for the support they had given him. Dr. Meltzer then delivered his valedictory address, 'Some Aspects of Cardiac Disease among the Bantu'.

IN MEMORIAM

DR. KURT COLSEN

Mr. M. K. Tucker, F.R.C.S. (Edin.), of Johannesburg writes: When Kurt Colsen landed in Cape Town in 1936 as a refugee from Nazi Germany, he had accepted his country of adoption through the turn of a card, because he and his friends in Europe had voluntarily decided that their Fatherland held no future for them under the existing regime, and they turned cards one evening to see where fate would send them.



Dr. Kurt Colsen

Kurt had no friends in South Africa, nor money, to help him—only his own high resolve, integrity and great friendliness.

Although he was a highly qualified orthopaedic and general surgeon in Germany, yet these attributes were of no value to him in South Africa until he could qualify for registration by graduating through a teaching hospital for the final 3 clinical years. This he was determined to do, and he set about making a living by representative selling for commercial firms, meanwhile learning the intricacies of the English language, of which he had been completely ignorant before landing in Cape Town.

Such was Kurt's force of character, and great love of his fellow beings, that he early on found many friends to share his trials, and he was able to achieve his ambition of enrolling as a medical student in Johannesburg in 1938. It was now that I first came to know Kurt when he attended the ward rounds in the hospital, and he quickly proved himself a courteous and reliable person. He found no difficulty in qualifying for registration in the minimum time required.

His first wish now was to join the army and serve wherever he could, and it was at this time that I again came to know him on the hospital ship in the Union Defence Forces. Eventually when we were demobilized, I found myself closely associated with him when we were both working in Professor Brebner's Unit at the Johannesburg Hospital.

From then onwards began a warm and satisfying association with Kurt, because his unfailing help and comradeship were always positive, and his very wide range of interests were a constant source of surprise and education. Quite apart from his very considerable ability as a surgeon, he was most keenly interested in people and their doings, so that he had an exceptionally wide circle of friends, all of them on an intimate Christian-name basis. His great vitality made him keenly interested in the theatre, where he was a confirmed 'first nighter', in antique collections, and in painting and music, to mention some of his hobbies.

In the professional world Kurt came to command the respect of his colleagues, for he was a courageous and skilled surgeon with a special aptitude for orthopaedic surgery, but his colleagues in the General Hospital, where he was appointed to the part-time staff, also knew him as a good sound general surgeon, working always with the greatest integrity, and in the interests of the profession and his patients. He was associated with me in the wards for the past 8 years, and I share a heavy feeling of loss with those of his colleagues who also worked with him.

As Secretary of the Association of Surgeons of South Africa, he proved a courteous and reliable executive, and showed his deep concern for the welfare of the profession. His private practice was large, and he was widely consulted by lawyers and insurance companies, who appreciated his integrity and sound common sense and lucidity of thought when they were settling claims in respect of their clients.

Kurt was an asset to the country of his adoption, and his teaching of students has been appreciated by numerous practising doctors of today. When the disease which finally caused his death first became manifest, he continued with his manifold duties and engagements, but had gradually to forego some of his social activities. He recently sought the advice of the leading authorities in the capitals of Europe, but he finally proved his love of his colleagues in South Africa by returning to Johannesburg to undergo the operation which had become imperative. Despite the great pain he was suffering towards the end, he nevertheless gave several lectures in Europe, which revealed the regard in which he was held.

My abiding memories of Kurt are of a great integrity, courage and love of humanity, and he will be most sadly missed. We can only assure his wife, Betty, and family that their great sorrow is shared by many others.

NEW PREPARATIONS AND APPLIANCES: NUWE PREPARATE EN TOESTELLE

NEUTRAPEN, A PENICILLINASE

At the Fifth Annual Symposium[1] on Antibiotics at Washington, D.C. in October 1957, Dr. Henry Welch, antibiotic officer of the American Food and Drug Administration, reported on a new drug which counteracts the harmful side-effects that sometimes follow the administration of penicillin. The drug has been named Neutrapen and is described as an injectible penicillinase. It was developed in the laboratories of Schen-labs Pharmaceuticals but was stated to be not yet on the market.

Dr. Welch said that a 4-year nation-wide survey, from 1953 to 1957, had shown an increase each year in serious allergic reactions to penicillin; it disclosed a substantially higher number of serious reactions to penicillin than to other antibiotics. Dr. Welch, however, emphasized that the number of cases showing side-effects is still small when it is considered that millions of persons receive penicillin each year, with a saving of tens of thousands of lives. The annual penicillin production in the USA was now said to total 325 tons. About 10% of the American population, or 17 million persons, were allergic to some degree to various substances in food, drugs and cosmetics. The penicillin allergy varied from 3 to 10% of the population. Skin testing to predetermine allergy has been unsuccessful.

The 4-year survey conducted by Dr. Welch was described as a geographic sampling of severe cases of side-effects to drugs. These drugs were handled by more than 1,600 private practitioners plus a sampling from the country's hospitals, and was made by Food and Drug Administration inspectors. The study of the case histories of severe reactions—especially those from penicillin given by intramuscular injection—shows there should be a clear-cut indication of need before penicillin is administered. In some cases, the injection of penicillin threatened the patient's life.

In reporting on test applications of the new drug, Dr. Murray G. Zimmerman, of the University of California, stated that the drug

was used on 52 patients with allergic reactions subsequent to penicillin injection. The new drug had been successful in nearly all of the cases, and in many cases complete clearing of side-effects took place within from 24 hours to a few days.

Dr. Zimmerman said that the penicillinase was an enzyme secreted by many strains of bacteria and that it resulted in total destruction of the allergy-producing substance in penicillin. One of five scientists reporting on the success of penicillinase, Dr. Zimmerman called the new drug cheap, safe and easy to administer, and said that it corrects the cause by destroying the allergy-causing antigens rather than merely suppressing the symptoms.

[Penicillinase is being advertised in American medical journals. The advertisements state that this enzyme hydrolyses penicillin to penicillinoic acid, which is not allergenic. One injection may be sufficient to clear most reactions in 12-96 hours. Itching abates promptly. It may be life-saving in anaphylactic reactions, though it may not be capable of overtaking the severe shock that sometimes follows immediately upon a penicillin injection. The dose suggested is 800,000 units.—Editor.]

1. Radioscript, American Chemical Society News Service, October 1957.

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ELTHER ELECTRONIC ELECTRO-SHOCK APPARATUS

Pharmedent Laboratories announce the Elther Electronic Electro-shock apparatus, Type E.S. (for Brief Stimulus Therapy).

Messrs. Cohen Stuart (Holland), after many experiments, have succeeded in building an apparatus that is ideal for so-called Brief Stimulus Therapy. They set themselves the task of finding a current type that could induce a complete shock with a manimum quantity of energy. This turned out to be a rectified current consisting of perfectly rectangular and very brief stimuli. In this apparatus the energy per unit of time is about 1/500th of that in normal alternating-current apparatus. The appliance offers the following advantages:

1. *Pulse duration of the direct-current stimuli.* The pulse-duration experiments, ranging from 8 millisec. to 1/20 millisec., proved the ideal value, which required least energy, to be near 1/10,000 sec.

2. *Frequency of the direct-current stimuli.* This frequency has been kept adjustable between 10 per sec. and 100 per sec. At a frequency of 10 per sec. a minimum amount of energy is sufficient. The narcosis shock (lasting about 7 minutes) requires a far higher frequency; in this case it is possible to increase the frequency gradually, instead of the tension. Increasing the tension has the disadvantage of leading up to a stridor. In resuscitating from barbituric and insulin comas, also an adjustable frequency is required.

3. *Electrodes.* These may be kept very small, because very small amounts of energy are used. This allows a better localization of the current.

4. *Time of introduction.* The current does not immediately reach its maximum value, but may increase steadily during an automatically controlled time (glissando effect). Together with the low energies, this ensures a shock of very smooth course. Fractures no longer occur.

5. *Automatic time switch.* The time during which the current passes through the brain is controlled electronically by a built-in automatic appliance.

6. *Adjustment and testing.* The apparatus may be adjusted beforehand by means of a built-in patient-resistance; preliminary testing is provided for to ensure that everything is in order.

7. *Servicing.* A push-button in one of the shock handles makes it possible for one person to operate the apparatus.

8. *Adjustment.* In spite of the wide range of possibilities offered by this apparatus, the adjustment and operation are surprisingly simple, thanks to the logically designed instrument panel.

9. *All methods* of shock treatment in use at present can be applied by means of this apparatus.

10. Mnemonic, inculcational and orientational disorders, which normally appear after electro-shock, treatment have almost completely vanished.

These appliances are installed at two wellknown mental institutions and are giving excellent results.

The local agents are Pharmedent Laboratories, P.O. Box 2316, Pretoria.

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'OTAMIDYL' EAR DROPS

Maybaker (S.A.) (Pty.) Ltd. announce the introduction of 'Otamidyl' brand antibacterial and antifungal ear drops, and supply the following information:

'Otamidyl' contains dibromopropamidine isethionate, 0·15% w/v, and diamidinodiphenylamine dihydrochloride, 0·5% w/v in propylene glycol. The antibacterial and antifungal properties of these compounds are retained in the presence of pus, blood, and tissue debris. Strains of organisms which are resistant to antibiotics are fully sensitive to the diamidines.

'Otamidyl' is indicated for use by topical application in the treatment of otitis externa and chronic suppurative otitis media.

PASSING EVENTS : IN DIE VERBYGAAN

Dr. D. v. d. Spuy, D.M.R., has started in practice as a Specialist Radiologist at Medical Centre, cor. Joubert Street and Senator Marks Avenue, Vereeniging. Telephones: rooms 642-5355, residence 854-3012.

Dr. D. v. d. Spuy, D.M.R., praktiseer as Spesialis-Radioloog te Mediese Sentrum, hoek van Joubertstraat en Senator Marks-laan, Vereeniging. Telefone: kamers 642-5355, woning 854-3012.

* * *

Dr. Lucie van Dam has resumed practice as a Specialist Psychiatrist at 43 Mill Park Road, Port Elizabeth, after having been away with illness since November. Telephone 69006.

* * *

Research Forum. The next meeting of Research Form, University of Cape Town, will be held on Tuesday 15 April at 12 noon, in the A-Floor Lecture Theatre, Groote Schuur Hospital, Cape Town. Speakers, Dr. J. D. L. Hansen and Dr. H. Schendel. Subject, 'Nitrogen Metabolism Studies in Kwashiorkor'.

* * *

Messrs. Squibb Laboratories have in recent months built up in Johannesburg an extensive library of 16 mm. medical sound films. Interested doctors are invited to apply for a complete list of the films, from which selections may be made, to Squibb Laboratories (Pty.) Ltd., P.O. Box 9975, Johannesburg. Telephone 449648. All films are available for private showings or association meetings free of charge.

* * *

Lede word daaraan herinner dat hulle die Sekretaris van die Mediese Vereniging van Suid-Afrika, Posbus 643, Kaapstad, sowel as die Registrateur van die Suid-Afrikaanse Mediese en Tandheelkundige Raad, Posbus 205, Pretoria, moet verwittig van enige adresverandering.

Versuim hiervan beteken dat die *Tydskrif* nie afgelewer kan word nie. Dit het betrekking op lede wat oorsee gaan sowel as dié wat binne die Unie van adres verander.

* * *

Dr. Jacques Roux, Gynaecologist and Obstetrician, has changed his home address to 7 Clarendon Road, Pinelands, Cape, where his new telephone number is 6-2606. His address and telephone number (3-5088) at his consulting rooms, 402/405 Medical Centre, Cape Town, remain unchanged.

Dr. Jacques Roux, Ginekoloog en Verloskundige, het van huisadres verander na Clarendonweg 7, Pinelands, Kaap, waar sy nuwe telefoonnommer 6-2606 is. Sy adres en telefoonnommer

(3-5088) hy sy spreekkamers te Mediese Sentrum 402/405, Kaapstad, bly onveranderd.

* * *

Union of South Africa. Department of Health. Notification of formidable epidemic diseases and poliomyelitis in the Union during the period 21-27 March 1958.

Plague, Smallpox, Typhus Fever: Nil.

Poliomyelitis

	Eur.	*Nat.*	*Col.*	*As.*	*Total*
Transvaal	6	4	–	–	10
Cape Province ..	1	3	–	–	4
Orange Free State ..	–	–	–	–	–
Natal	–	–	–	–	–
Totals ..	7	7	–	–	14

Local Authorities		*Eur.*	*Non-Eur.*
Transvaal:			
Johannesburg Municipality	U	2	
Klerksdorp District ..	R		1
Krugersdorp Municipality	U	2	
Pretoria Municipality ..	U	1	1
Rustenburg Municipality	U	1	
Springs District	R		1
Witbank District	R		1
Cape Province:			
Cape Town Municipality	U	1	
Cradock Municipality ..	U		1
Port Elizabeth Municipality	U		2
Orange Free State and Natal		Nil	

U = Urban. R = Rural.

The Third World Congress on Fertility and Sterility, sponsored by the International Fertility Association, will be held in Amsterdam, Holland, on 7-13 June 1959. The general outlines of the sections will be as follows: (1) Female sterility (physiology of reproduction, pathology, endocrinology, clinical problems, treatment. (2) Male sterility (physiology of reproduction, pathology, endocrinology, clinical problems, treatment). (3) Basic research and/or animal reproduction. (4) Psycho-sexual problems.

Priority will be given to papers concerning the following subjects: (1) Embryonic death (aetiology, pathogenesis, placental structures in relation to the condition of the foetus, functional problems and diagnosis of the embryonic and foetal death, and habitual abortion); (2) Hormonal factors and vitamins in fertility and sterility (ovulation and sterility, induction of ovulation, influence of thyroid, steroids etc. on ovulation, influence and physico-pathological significance of vitamins, hormones and spermatogenesis, vitamins and spermatogenesis); (3) Relative value of the techniques for study of the endocrine functions in human sterility (study of the oestrogen function, study of the luteal function, study of the adeno-hypophysis function, testicular biopsy value, study 'in vitro' of the fertilization of mammalian and human ovums, use of radio-isotope designers in the study of the sexual function); (4) Biochemistry of spermatogenesis; (5) Psycho-sexual problems in sterility.

The official languages will be English, French, German, Spanish (with simultaneous translation). Registration fee 40 dollars (accompanying family-members 15 dollars). After January 1959, the registration fee will be 50 dollars. Titles for papers should be sent not later than June 1958 to both Dr. Alfonso Alvarez-Bravo, Avenida Horacio 1506, Mexico City, D.F., Mexico, chairman, and Prof. D. S. ten Berge, Academisch Ziekenhuis, Groningen, Holland, executive member of the Programme Committee. For further information and registration apply to Dr. L. I. Swaab, Hon. Secretary, Third World Congress on Fertility and Sterility, Sint Agnietenstraat 4, Amsterdam-C. or to the nearest Wagons Lits/Cook office.

REVIEWS OF BOOKS : BOEKRESENSIES

DEAF, MUTE AND MENTALLY DEFICIENT CHILDREN

Deafness, Mutism and Mental Deficiency in Children. By Louis Minski, M.D., F.R.C.P., D.P.M. Pp. viii + 82. 13 Figures. 12s. 6d. net. London: William Heinemann—Medical Books—Ltd. 1957.

Contents: Preface. I. General Aspects of the Problem. II. Clinical Data. III. Lay-out and Staffing of the Units. IV. General Methods of Assessment. V. Audiometry. VI. Electrophysiological Methods of Assessment. VII. Psychological Testing. VIII. Discussion of the Problem. Index.

In children it is often very difficult to distinguish between those with mental defects and those who are deaf and maladjusted, or have no speech and are not deaf. As the author of this book points out, it is important to make a diagnosis, for in the one case little can be done, while in the other, proper education can help to make a normal individual of one who otherwise might spend his life in a mental institution. The diagnosis may be particularly difficult in the child suffering from cerebral palsy, and here too a correct diagnosis is all-important for the child's future.

This book is a survey of Dr. Minski's experiences at two institutions with which he has been closely associated. In the unit at Belmont Hospital, children are investigated as thoroughly and as quickly as possible in an attempt to arrive at a diagnosis, and are then recommended for, or placed in suitable schools. At such a unit the child can be adequately assessed, and not 'dismissed in a perfunctory manner following a single out-patient examination'.

The unit at Sutton is a residential home, run by a foster-mother. It admits deaf children who are deprived of affection and security and require long term treatment to remove their emotional difficulties. It also caters for those children who have had no previous education, as so often happens in this situation.

The author describes the various methods of assessment used by their units e.g., audiometry, electro-encephalography, and psychological testing, and discusses their value. One is left with the impression that though the work is tedious and difficult, it is well worth the effort.

There is much valuable material in this small but 'meaty' book, and I recommend it particularly to paediatricians, otologists and school medical officers.

A bibliography, supplemented by other useful reading material, would be a useful addition in future editions.

I.M.

EDEN AND HOLLAND'S OBSTETRICS

Eden & Holland's Manual of Obstetrics. 11th Edition. By Alan Brews, M.D., M.S., M.R.C.P., F.R.C.S., F.R.C.O.G. Pp. xii + 751. 61 Plates, 12 in Colour and 371 Illustrations in the Text. 63s. net. London: J. & A. Churchill Ltd. 1957.

Contents: Part I. Normal Pregnancy. Sex Cycles, Ovarian and Uterine. Sex Hormones, Ovarian, Pituitary and Placental. Maturation and Fertilization of the Ovum. Early Development of the Zygote (Fertilized Ovum). Implantation of Zygote, Decidual Formation, Chorion. Amnion, Umbilical Cord and Foetus. Circulation, Blood Formation and General Physiology in the Foetus. The Gravid Uterus. Maternal Physiology. Diagnosis. Normal Duration. Multiple Pregnancy. Antenatal Care. *Part II. Abnormal Pregnancy.* Common Discomforts. Hyperemesis Gravidarium. Abortion: Miscarriage. Uterine Moles. Extra-Uterine (Ectopic) Gestation. Infections of the Urinary Tract. Anaemias. Blood Incompatibilities. Glycosuria: Diabetes Mellitus. Specific Toxaemia. Essential Hypertension. Chronic Nephritis. Eclampsia. Jaundice: Icterus Gravis Gravidarium. Generalized Infections. Venereal Diseases. Respiratory Diseases. Cardiovascular Diseases. Endocrine Disorders. Neurological and Psychological Disorders. Dermatological Disorders. Developmental Anomalies, Displacements of Genital Tract. Infections of Genital Tract. Tumours of Genital Tract. Hydramnios and Diseases of Placenta. Abnormalities of Embryo and Foetus. *Part III. Normal Labour.* Onset. Stages. Anatomy and Physiology of 1st and 2nd Stages. The Foetus. The Forces. Anatomy and Physiology of the 3rd Stage. Mechanism. Management. Control of Pain. Uterine Stimulants. Delivery of Foetus and Placenta. Nursing Care after Delivery. *Part IV. Abnormal Labour.* Occipito-posterior Positions of the Vertix. Face and Brow Presentations. Breech Presentations. Transverse Lie. Twin Labour. Prolapse of Cord and Limbs. Pelvic Contraction: Aetiology and Varieties. X-ray Pelvimetry. Contracted Pelvis. Management of Delivery. Ovarian and Uterine Tumours. Rigidity of Cervix and Pelvic Floor. Abnormality of Uterine Action. Obstructed Labour. Maternal Injuries in Parturition. Ante-partum Haemorrhage and Placentography. Post-partum Haemorrhage. *Part V. The Puerperium.* General Physiology. Management. Infection. Inflammation of Breasts. Chorionepithelioma. Mental Disorders. Unexpected Death (or Near Death). *Part VI. The Foetus.* Pulmonary Respiratory Peri-natal Asphyxia (Foetal and Neonatorum). Intra-Uterine and Post-nata.

Death. Cranial Injuries. *Part VII. The Newly-born Child.* Breast Feeding. Artificial Feeding. Early Progress. Management of Prematurity. Digestive Disturbances. Birth Injuries. Disorders. *Part VIII. Obstetric Operations.* Induction of Abortion. Induction of Labour. Version. Obstetric Forceps. Caesarean Section. Destructive Operations on Foetus. Pubiotomy and Symphysiotomy. *Part IX.* Maternal Mortality and Morbidity. The Maternity Service. *Appendices.* 1. Diet during Pregnancy and Lactation. 2. Antenatal and Postnatal Exercises. Physiotherapy. 3. Social Care of Women in Pregnancy. 4. Emergency Obstetric Units. Index.

Eden and Holland's textbook has always been an excellent manual for both the undergraduate and the postgraduate student. The present edition which has been brought up to date by editor Alan Brews is certainly no exception to the previous editions.

Chapter I on normal pregnancy, is very well written and is most probably the best chapter in the book. Chapter 2 is rather the exception, in that the classification of abnormalities in pregnancy is rather disjointed and could be improved upon, to make it less confusing to the student. Most subjects are touched upon, and the medical complications of pregnancy could be more clearly elucidated. The chapter on normal labour is clear and concise and the obstetrical mechanisms from the point of view of the undergraduate clearly explained. Profuse and well selected illustrations greatly assist in understanding the text.

Chapter 7 on the newly born child is again contributed by R. H. Tallerman, and is packed with practical information in necessary detail, which is so often overlooked.

An appendix on Emergency Obstetrical Units has been added. A particularly useful feature which is maintained, is the guide to further reading which follows each chapter. This includes the literature from the most recent journals.

Much new material has been included. The contributions which are models of simplicity and easy reading, can hardly fail to stimulate further any student or doctor with an interest in Obstetrics.

J.A.

HISTORY OF PSYCHIATRY

Roots of Modern Psychiatry—Essays in The History of Psychiatry. By Mark D. Altschule, M.D. Pp. viii + 184. 15 Figures. $5·75. New York and London: Grune & Stratton, Inc. 1957.

Contents: Preface. 1. Ideas About Anxiety Held by Eighteenth-Century British Medical Writers. 2. The Pineal Gland: Memory Valve or Seat of the Soul? 3. Broussais and Griesinger: The Introduction of Ego-Psychology into Psychiatry. 4. The Growth of the Concept of Unconscious Cerebration before 1890. 5. Allegorical Somatognosy and Psychosomatic Medicine. 6. Venus Ascendant. 7. The Concept of Civilization as a Social Evil in the Writings of Mid-Nineteenth-Century Psychiatrists. 8. Eclecticims in the Treatment of Mental Disease in the Nineteenth Century. 9. Greek Revival.

Dr. Altschule has written a source book of the history of Psychiatry. His own comments are succinct and to the point, and he allows us to enjoy a large number of quotations from a considerable number of authors. His selections vary from the Yellow Emperor's book on Medicine (*ca.* 2600 B.C.) to excerpts from Tuke, Griesinger and Maudsley, and they also include a stimulating number of quotations from the ancients. His history goes up to Freud but no further: Jung is only mentioned twice and Adler not at all, and the more modern developments from 1910 onwards are not included, but we must be grateful for what we have been given, as this is undoubtedly one of the best books of its kind so far published.

Of particular interest are the chapters on the concept of the unconscious and that on the introduction of the Ego into psychology. Many of the ideas which are commonly considered to be original in Freudian psychology are found to have been used long previously—this does not detract from their value in any way, although Dr. Altschule is far from being polite about Freudianism.

There are many pithy quotations: James on the Unconscious, 'between the unconscious and the conscious state lies a distinction which is the sovreign means of believing what one likes in psychology, and the turning of what might become a science into a tumbling-ground for whimsies.' Esquirol on Gall, when the latter was asked first to study the heads of patients and then characterise their illness from this phreniological approach,' at that Gall became mute; he had been able, with complete certitude, to relate the effect to the cause; but from the cause he could not descend to the effect.'

And in the ingenuous pronouncements of some of the medical fathers there is much that is amusing. Gilles de Corbeil (XII Cent.) specifically recommend a love affair, not as a remedy for melancholy, but as a cure for megalomania.

Dr. Altschule is well able to coin an aphorism himself, as when he says, 'many entirely sublimate their drive towards vigorous exercise by means of sexual activity—the only form of vigorous exercise that is still indulged in by adult inhabitants of American cities.'

Finally, for those who are impressed by the Greek roots of Freud's theories there are some disturbing references pointing to 'careless evaluation of evidence, slovenliness of scholarship, and poverty of invention.'

Whether one is a Freudian or an eclectic this book is a valuable book of concise reference and a corrective to much that was woolly in our minds.

J.M.M.

DIAGNOSIS AND TREATMENT OF VASCULAR DISORDERS

Diagnosis and Treatment of Vascular Disorders. Edited by Saul S. Samuels, M.D. with seventeen contributors. Illustrations. Pp. viii + 621. $16·00. Baltimore: The Williams and Wilkins Company. 1957.

Contents: 1. *The Anatomy of the Peripheral Circulation.* by Lawrence N. Atlas, M.D. 2. *The Innervation of the Peripheral Blood Vessels.* by Lawrence N. Atlas, M.D. 3. *Physiology of Sympathetic Innervation of Peripheral Blood Vessels.* by David I. Abramson, M.D. 4. *Examination of the Patient.* by R. H. Goetz, M.D. 5. *Angiography* by Frederick B. Wagner, M.D. 6. *Local Cold Injuries* by Harris B. Shumacker, Jr., M.D. and Robert E. Lempke, M.D. 7. *Arterial Injuries* by F. A. Simeone, M.D. 8. *Senile Obliterative Arteritis (Arteriosclerosis Obliterans)* by A. M. Boyd, F.R.C.S. and A. H. Ratcliffe, B.Sc. 9. *Arteriosclerosis—Atherosclerosis in Relation to Diabetes* by David W. Kramer, M.D. and Paul K. Perilstein, M.D. 10. *Endarteritis Obliterans* by David W. Kramer, M.D. 11. *Treatment of Gangrene of the Extremities.* by Saul S. Samuels, M.D. 12. *Thromboangiitis Obliterans* by Saul S. Samuels, M.D. 13. *Raynaud's Disease and Raynaud's Phenomenon* by R. H. Goetz, M.D. 14. *Erythermalgia* by R. H. Goetz, M.D. 15. *Arterial Aneurysms* by Murry G. Fischer, M.D. 16. *Arteriovenous Fistulae* by R. H. Goetz, M.D. 17. *Embolism and Thrombosis* by George H. Yeager, M.D. 18. *Anticoagulant Therapy* by Shepard Shapiro, M.D. 19. *Varicose Veins* by Egmont J. Orbach, M.D. 20. *Glomus Tumors* by R. H. Goetz, M.D. 21. *The Scalenus Anticus Syndrome* by George H. Yeager, M.D. 22. *Chronic Edema of the Legs* by S. S. Rose, M.D. 23. *Periarteritis Nodosa* by David W. Kramer, M.D. and Paul K. Perilstein, M.D. 24. *Medical Legal Aspects* by Saul S. Samuels, M.D.

There is in this volume a wealth of varied experience and informed opinion on many aspects of peripheral vascular disease.

The first three chapters cover the relevant fields of anatomy, innervation, and physiology. In the latter section the reader might be reminded that fact and theory based on animal experiment should not necessarily be assumed to apply clinically to man. The illustrations, particularly those on collateral venous circulation are useful, though perhaps over reduced in size.

The section on the examination of the patient is practically a monograph, and incorporates a critical survey of the range of specialized mannoeuvre's available for estimating peripheral circulation.

The field of angiography is widely covered, together with the indications and basic techniques for various investigations. The contributor does not shy away from a description of the hazards and complications. In the section on varicose veins there is included, though not necessarily advocated, some dubious therapy, such as subcutaneous vein ligation and sclero-therapy in pregnancy.

With so many contributors it follows that changes of style and approach disrupt the continuity of the book, and provide considerable overlap. These detractions are offset by the monographic structure of the chapters and the individuality of differering opinions.

J.D.S.

MANUAL OF ANAESTHESIA

Anesthesia: A Manual for Students and Physicians. Fifth Edition. By Stuart C. Cullen, M.D. Pp. 295. 37 Figures. $5·50. Chicago: Year Book Publishers, Inc. 1957.

Contents: 1. Use of Depressant Drugs. 2. Airway. 3. Ventilation. 4. Inhalation Anesthesia: Agents. 5. Inhalation Anesthesia: Technics. 6. Spinal Analgesia. 7. Regional, Infiltration and Topical Analgesia. 8. Signs of Anesthesia. 9. Choice of Anesthetic Agent and Technic. 10. Recognition and Treatment of Shock. 11. Oxygen Therapy. 12. Pre- and Post-anesthetic Care of the Patient. 13. Explosions Hazards. Appendix: Anesthetic Agents Available for Office Use. Index.

In his preface, the author states that the material has been 'directed at assisting the student and physician in acquiring a basic approach to the solution to the problems of anaesthesia'. He has succeeded admirably. It would be naive to state that this or that book is 'The best' but this book could certainly be called a winner.

The first chapter—The use of depressant drugs— immediately gains attention by the recognition of the many undesirable effects of the narcotics, and by an attack on ritual and routine opiate

premedication. This latter is only too commonly, and almost universally practised. The sensible step by step treatment of drug depression, as outlined, could well be copied, framed and hung in any casualty department for the guidance of both interns and their elders.

A measure of the author's realistic and practical approach to the subject is seen by the fact that nearly one third of the book is occupied by sections on depressant drugs, maintenance of airway and ventilation, before any attempt is made to describe agents or techniques. In the chapter on ventilation the author repeatedly emphasises the importance of adequate ventilation—not only to maintain oxygenation, but to eliminate the hidden enemy, carbon dioxide.

Whilst this book might be disappointing to the enthusiastic 'Do it yourself' practitioner who occasionally administers anaesthetics, and seeks dogmatic descriptions of technique, it can be unreservedly recommended to any serious student,—practitioner or anaesthetist attempting to gain an insight into many of the problems of anaesthesia.

P.J.

TEXT BOOK OF RADIO-DIAGNOSIS

A Text-book of X-ray Diagnosis. By British Authors in Four Volumes. Third Edition. Edited by S. Cochrane Shanks M.D., F.R.C.P., F.F.R. and Peter Kerley, C.V.O., C.B.E., M.D., F.R.C.P., F.F.R., D.M.R.E. Volume I. Head and Neck. Pp. xii + 521. 533 Illustrations. £4 10s. net. London: H. K. Lewis & Co. Ltd. 1957.

Contents: List of Contributors. Preface. Summary of Contents. *Part One. Central Nervous System.* I. General Technique and Pathology. II. The Radiological Features of the Cranium, Normal and Pathological. III. Ventriculography and Encephalography. IV. Cerebral Angiography. V. Intracranial Lesions. VI. Anomalies and Diseases of the Skull. VII. The Spinal Cord. *Part Two. The Teeth and Jaws.* VIII. The Normal Teeth and Jaws. IX. Unerupted and Supernumerary Teeth. X. Inflammatory Diseases of the Periodontal Membrane and Alveolus. XI. Injuries to the Teeth and Jaws. XII. Cysts and Tumours of the Teeth and Jaws. XIII. Inflammatory and other Diseases of the Jaws. XIV. Diseases of the Temporo-Mandibular Joint and Antrum. *Part Three. The Eye.* XV. The Eye. *Part Four. The Accessory Nasal Sinuses.* XVI. General Considerations, Anatomy and Physiology. XVII. Aetiology of Inflammatory Disease of the Sinuses. XVIII. Radiographic Technique. XIX. The Use of Iodised Oil in the Diagnosis of Nasal Sinus Disease. *Part Five. The Ear and Temporal Bone.* XXI. General Considerations and Development. XXII. Anatomy, Physiology and Pathology. XXIII. Radiographic Technique. XXIV. Radiological Interpretation. Index.

It is now 20 years since the first edition of the British Author's Textbook of Radiology made its welcome appearance. It was a modest three volume edition in those days and it was not until 1950—despite the War and all the setbacks which it implied—that the enlarged four volume, second edition emerged.

The third edition is now here, again in four volumes. The pages, however, are larger and in this, the first volume on the head and neck, the whole work has been increased in size. New contributors are at work and a better selection of illustrative radiographs has been employed. The text has also undergone some changes, here again with benefit to the whole work.

The subject they endeavour to cover is enormous and is expanding daily. It is no longer possible to deal in detail with all the ramifications of radiodiagnosis in four volumes. Volume One, therefore, largely provides the main basic information needed to study the head and neck reasonably well, but not comprehensively. The bibliography provided at the end of each chapter should prove sufficiently exhaustive for most searchers.

The section in which the greatest improvement is evident, when compared with the previous editions, is that dealing with Cerebral Angiography. Even so, it is still only accorded a bare 60 pages, much of which is devoted to illustration. It is clearly not possible to do anything like full justice to such a subject in such a small compass.

The problem of negative or positive illustrations still persists. Throughout the section dealing with Jaws and Teeth, the X-rays presented really look like X-rays i.e. bones, teeth etc., are white and air and soft tissues, black, which is surely preferable (to the reviewer at any rate), than the exact opposite, for no one who studies radiographs has any time or feel for positives.

There is, however, no doubt that it is pleasant to see the 'Bible' of British Radiology reappearing. Doubtless, too, it will find its rightful way on to the shelves of most students of radiodiagnosis as well as into the reference libraries of practicing radiologists, and for these purposes, it can be highly recommended.

L.J.

BAILLIÈRE'S NURSES' DICTIONARY

Baillière's Nurses' Dictionary. Fourteenth Edition. Revised by Barbara F. Cape, S.R.N., S.C.M., D.N. (Lond.). Pp. xi + 526. Illustrations. 6s. 6d. London: Baillière, Tindall and Cox Ltd. 1957.

Contents: Foreword. Preface. Dictionary of Medical Terms. Appendices. I. Surgical Instruments and their Care. II. Materials Used as Sutures and Ligatures. III. Anaethesia. Anaesthetics. Analgesia in Midwifery. IV. Oxygen Therapy. V. Static Electricity and Antistatic Precautions. VI. Technique for Ward Dressings. VII. Transfusion of Blood and Other Fluids. VIII. Diagnostic Radiography. IX. Radiotherapy. X. Urinary Tract Investigations. Abnormalities in Urine. Chemical Tests. XI. Antiseptics and Disinfectants in Common Use. XII. Chemotherapeutic and Antibiotic Drugs. XIII. Common Drugs and Dosages. XIV. Methods of Giving Drugs. XV. Legal Control of Poisons for Medical Use. XVI. Poisoning. XVII. First Aid Treatment. XVIII. Splints, Bandages and Bandaging. XIX. Dietetics. XX. Average Weight and Height of Children. XXI. Weights and Measures. XXII. Thermometers. XXIII. Abbreviations of Medical Terms. XXIV. Degrees, Diplomas, Organizations, etc. XXV. A Short Directory of Useful Addresses.

This little dictionary for nurses is in a convenient pocket size, yet it includes all the terms which a nurse need know, amongst which will be found the newest and most modern. In spite of its very full scope, space is found for line drawings to illustrate certain terms where necessary.

It is a dictionary which can be recommended with confidence not only to nurses but also to members of Red Cross, St. Johns and other similar organisations.

A.H.T.

CORRESPONDENCE : BRIEWERUBRIEK

OSTEOPOROSIS AND SCURVY AMONGST AFRICANS

To the Editor: At a clinical meeting at Coronation Hospital[1] a patient was shown who was suffering with osteoporosis of the spine; he also had a swollen leg thought to be due to scurvy. The association of acute scurvy with radiological evidence of osteoporosis of the skeleton is a syndrome quite commonly observed in the Bantu. We have recently reported 16 such cases.[2] It has long been known that experimental scurvy produces osteoporosis in guinea-pigs; although it is assumed that vitamin-C deficiency is a factor in the aetiology of human osteoporosis few if any convincing examples have been reported.

In our paper we drew attention to the facts that osteoporosis in these Bantu subjects occurred in a disproportionate number of males and in comparatively young age-groups. Not all patients with osteoporosis showed overt signs of acute scurvy, but some suffered from haemorrhagic effusions which may have been scorbutic equivalents and others bore the stigma of chronic scurvy.

In a few patients there was no history or clinical evidence of scurvy. Moreover it was necessary to explain how an acute disease could produce chronic changes in bone. From the evidence we collected it seems quite likely that when its manifestations are not startling or disabling scurvy often goes unnoticed by the patient. For this reason it seemed probable that Bantu patients with osteoporosis suffered repeated minor attacks of scurvy or from chronic vitamin-C deficiency.

H. Grusin
E. Samuel

113 Lister Building
Jeppe Street
Johannesburg
28 March 1958

1. Report (1958): South African Orthopaedic Association, Clinical Meeting, case 5. S. Afr. Med. J., 32, 303 (15 March).
2. Grusin, H. and Samuel, E. (1957): Amer. J. Clin. Nutr., 5, 644.